541 General Session, Sat, 10:00 AM-11:30 AM and Poster Session (Board #D2), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM

TIVO-3: A phase III, randomized, controlled, multicenter, open-label study to compare tivozanib to sorafenib in subjects with refractory advanced renal cell carcinoma (RCC).

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Background: Tivozanib (T) is a biochemically potent and highly selective VEGF tyrosine kinase receptor inhibitor in clinical development in RCC. The TIVO-1 trial in treatment naïve or prior cytokine-treated subjects with metastatic (m) RCC showed a median progression free survival (mPFS) of 11.9 months (mos) for T compared to 9.1 mos for sorafenib (S) (p = 0.042, HR = 0.797). However, overall survival (OS) favored sorafenib, likely due to imbalanced crossover to active treatments. TIVO-3 was conducted to confirm the PFS results from TIVO-1. **Methods:** Subjects with mRCC who failed 2 or 3 prior systemic regimens, one of which included a VEGFR TKI other than S or T, were stratified by IMDC risk category and type of prior therapy (two TKIs; TKI plus checkpoint; TKI + other) then randomized in a 1:1 ratio to T or S. The primary objective was to compare PFS by blinded independent radiological review. 350 subjects were enrolled to yield 244 events with ~88% power to detect a difference of 6 mos vs. 4 mos with a two-sided p-value of 0.05 by the log-rank test. Secondary endpoints were OS, safety, objective response rate (ORR), and duration of response. **Results:** The two arms were well balanced for demographics and prior cancer history.60% of subjects had 2 prior lines of therapy and 40% had 3 prior lines. 28% had prior treatment with a checkpoint inhibitor. T demonstrated a statistically significant improvement in mPFS compared to S, 5.6 (95% CI 7.3-5.3) v. 3.9 mos (95% CI 5.6-3.7; HR 0.73; p=0.02). PFS rate at 2 years was 18% for T compared to 5% for S. ORR was 18% for T compared to 8% for S. 44% of T treated subjects experienced a grade 3 treatment-related adverse event compared to 55% for S. Subjects on T were less likely to require a dose reduction (24% v. 38%), interruption (48% v. 63%), or discontinuation (21% v. 29%) due to an adverse event than subjects on S. **Conclusions:** T is superior to S as measured by PFS; 2-year PFS, and ORR in this pre-treated population and is better tolerated than S. OS data will be updated prior to presentation. Clinical trial information: NCT02627963.

542 General Session, Sat, 3:45 PM-5:00 PM and Poster Session (Board #D3), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM

Safety and efficacy of nivolumab in metastatic renal cell carcinoma (mRCC): Final analysis from the NIVOREN GETUG AFU 26 study.

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Background: NIVOREN GETUG AFU 26 study, is a French multicenter prospective study to evaluate safety and efficacy of Nivolumab (N) in a broad "real world setting" in mRCC after failure of 1 or 2 tyrosine kinase inhibitors. **Methods:** Between February 2016 and June 2017, 729 pts have been enrolled across 27 institutions. Primary objective of the trial was safety assessed by grade ≥ 3 treatment related adverse event (TRAE). **Results:** Overall, 720 patients treated with N were included in this final analysis. All pts had clear cell mRCC. Median age was 64 years old, 77.4% were male, 84.7% had prior nephrectomy. ECOG PS was >1 in 15.0%, 21.3% pts had received prior everolimus, 22.4% pts had received more than 2 previous lines, IMDC risk groups were 18.3%/56.2%/25.5% for good/intermediate and poor risk respectively. Brain Metastasis at screening was noted in 83 (12.3%) pts. With a median follow up of 20.9 months (mo), median duration of treatment was 5.2 mo (0.5; 28.1) with 15% of pts still on therapy. Median PFS was 3.2 IC 95% [2.9; 4.6] mo. At the time of this analysis, 316 pts have died and 12 mo OS rate was 69% IC 95% [66; 73]. Objective response rate was 20.8% (1.2% CR, 19.6%PR). Stable disease was seen in 31.6% and PD in 47.6%. Noteworthy, 46.1% of pts were treated beyond progression. Overall, 123 pts (17.1%) have presented at least one grade ≥ 3 TRAE, including asthenia (2.4%), metabolic disorders (2.1%), gastro-intestinal disorders (1 .9%), musculoskeletal (1.7%), renal disorders (1.3%), hematologic (1.3%). 6 patients have developed grade 5 toxicity (2 cardiac failure, 1 macrophage activation syndrom, 1 Cerebral hemorrhage, 1 unknown). Treatment discontinuation due to any grade TRAE occurred in 54 pts (7.5%). Interestingly, pts with grade ≥ 3 TRAE had longer PFS than pts without grade ≥ 3 TRAE (HR 0.69 [0.55-0.87]). **Conclusions:** We report the primary objective analysis of the largest prospective real world setting study of N in mRCC. NIVOREN study demonstrates that N safety and efficacy in a "real world" prospective study are similar to the pivotal study. Grade ≥ 3 TRAE was associated with longer PFS. Clinical trial information: NCT03013335.

543 Oral Abstract Session, Sat, 2:00 PM-3:30 PM and Poster Session (Board #D4), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM

Pembrolizumab (pembro) plus axitinib (axi) versus sunitinib as first-line therapy for locally advanced or metastatic renal cell carcinoma (mRCC): phase III KEYNOTE-426 study.

Thomas Powles, Elizabeth R. Plimack, Viktor Stus, Rustem Airatovich Gafanov, Robert E. Hawkins, Dmitry Nosov, Frederic Pouliot, Boris Yakovlevich Alekseev, Denis Soulieres, Bohuslav Melichar, Ihor Vynnychenko, Anna Kryzhanivska, Igor Bondarenko, Sergio Jobim Azevedo, Delphine Borchiellini, Qiong Shou, Rodolfo F. Perini, Mei Chen, Michael B. Atkins, Brian I. Rini; Barts Health and the Royal Free NHS Trusts, Barts Cancer Institute, Queen Mary University of London, London, United Kingdom; Fox Chase Cancer Center, Philadelphia, PA; Department of Urology State Institution: Dnipropetrovsk Medical Academy under the MHU on the base Dnipropetrovsk I.I. Mechnykov Regional Clinical Hospital, Dnipropetrovsk, Ukraine; Russian Scientific Center of Roentgenoradiology, Moscow, Russian Federation; The Christie NHS Foundation Trust, Manchester, United Kingdom; Central Clinical Hospital, Moscow, Russian Federation; CHU de Québec and Laval University, Quebec, QC, Canada; P. A. Herzen Moscow Oncology Research Institute, Ministry of Health of the Russian Federation, Moscow, Russian Federation; University of Montreal, Montreal, QC, Canada; Department of Oncology, Palacky University Medical School and Teaching Hospital, Olomouc, Czech Republic; Sumy State University, Sumy Regional Clinical Oncology Center, Sumy, Ukraine; Ivanko-Frankivsk National Medical University, Ivano-Frankivsk, Ukraine; Dnepropetrovsk State Medical Academy, Dnepropetrovsk, Ukraine; UPCO - Hospital de Clinicas de Porto Alegre, Porto Alegre, Brazil; Centre Antoine Lacassagne, Nice, France; MSD China, Beijing, China; Merck & Co., Inc., Kenilworth, NJ; Georgetown Lombardi Comprehensive Cancer Center, Washington, DC; Cleveland Clinic Taussig Cancer Institute, Cleveland, OH

Background: A phase 1b study of pembro (anti–PD-1) plus axi (VEGFR-TKI) showed promising antitumor activity and manageable safety in patients (pts) with previously untreated mRCC. The global, open-label, phase 3 KEYNOTE-426 study assessed the efficacy and safety of pembro + axi vs sunitinib as first-line therapy for mRCC (NCT02853331). **Methods:** Eligible pts with clear-cell mRCC, no previous systemic therapy for mRCC, and KPS ≥70% were randomized 1:1 to pembro 200 mg IV Q3W for a maximum of 35 cycles plus axi 5 mg orally BID or sunitinib 50 mg orally QD (4-wk on/2-wk off schedule). Treatment was given until PD, intolerable toxicity, or pt/investigator decision. Randomization was stratified by IMDC risk group and geographic region. Primary endpoints were OS and PFS (RECIST v1.1 by blinded, independent central review [BICR]). ORR was the key secondary endpoint. At the protocol-specified first interim analysis, the superiority thresholds were $P = 0.0001$ for OS, 0.0013 for PFS, and 0.025 for ORR (if OS and PFS were significant). **Results:** 861 pts were randomized: 432 to pembro + axi, 429 to sunitinib. After a 12.8-mo median follow-up, 59.0% of pts in the pembro + axi arm and 43.1% in the sunitinib arm remained on treatment. Pembro + axi significantly improved OS (HR 0.53 [95% CI 0.38-0.74]; $P < 0.0001$; 12-mo rate 89.9% vs 78.3%), PFS (HR 0.69 [95% CI 0.57-0.84]; $P = 0.0001$; median 15.1 vs 11.1 mo), and ORR (59.3% vs 35.7%; $P < 0.0001$). Duration of response was prolonged with pembro + axi (median not reached vs 15.2 mo). The pembro + axi benefit was observed in all subgroups tested, including all IMDC risk and PD-L1 expression subgroups. Treatment-related AEs were grade 3-5 in 62.9% of pts in the pembro + axi arm vs 58.1% in the sunitinib arm and led to regimen discontinuation in 6.3% vs 10.1%. **Conclusions:** Pembrolizumab + axitinib provided superior OS, PFS, and ORR compared with sunitinib and had manageable safety in pts with previously untreated, advanced or metastatic clear-cell RCC. These data suggest that pembrolizumab + axitinib should be a new standard of care for this population. Clinical trial information: NCT02853331.

544 Oral Abstract Session, Sat, 2:00 PM-3:30 PM and Poster Session (Board #D5), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM

Subgroup analysis from JAVELIN Renal 101: Outcomes for avelumab plus axitinib (A + Ax) versus sunitinib (S) in advanced renal cell carcinoma (aRCC).

Toni K. Choueiri, Robert J. Motzer, Matthew T. Campbell, Boris Y. Alekseev, Motohide Uemura, Christian K. Kollmannsberger, Gwenaelle Gravis, Georg A. Bjarnason, Howard Gurney, Jinsoo Chung, John B. A. G. Haanen, Brian I. Rini, James M. G. Larkin, Manuela Schmidinger, Franco Nole, Aleksander Chudnovsky, Bo Huang, Subramanian Hariharan, Alessandra di Pietro, Laurence Albiges; The Lank Center for Genitourinary Oncology, Dana-Farber Cancer Institute and Brigham and Women's Hospital, Boston, MA; Memorial Sloan Kettering Cancer Center, New York, NY; The University of Texas MD Anderson Cancer Center, Houston, TX; Moscow Scientific Research Oncology Institute, Moscow, Russian Federation; Osaka University Hospital, Osaka, Japan; British Columbia Cancer Agency, Vancouver, BC, Canada; Institut Paoli-Calmettes, Marseille, France; Odette Cancer Centre Sunnybrook Health Sciences Centre, Toronto, ON, Canada; Macquarie University, Sydney, NSW, Australia; National Cancer Center, Goyang-Si, Korea, Republic of (South); Netherlands Cancer Institute, Amsterdam, Netherlands; Cleveland Clinic, Cleveland, OH; Royal Marsden NHS Foundation Trust, London, United Kingdom; Medical University Vienna, Department of Medicine I, Clinical Division of Oncology and Comprehensive Cancer Center, Vienna, Austria; Istituto Europeo Di Oncologia Medical Oncology Division of Urogenital and Head & Neck Tumours, Milano, Italy; Pfizer Inc., Cambridge, MA; Pfizer Inc., Groton, CT; Pfizer Inc., New York, NY; Pfizer SRL, Lombardia, Italy; Institut Gustave Roussy, Villejuif, France

Background: In the ongoing phase 3 JAVELIN Renal 101 trial, progression-free survival (PFS) was longer (median, 13.8 vs 8.4 mo; hazard ratio, 0.69; p=0.0001) and the objective response rate (ORR) was higher (51% vs 26%) with A + Ax vs S in patients with previously untreated aRCC. Here we report outcomes from an analysis of several prespecified subgroups. **Methods:** Patients were randomized 1:1 to receive A (10 mg/kg) IV every 2 weeks + Ax (5 mg) PO twice daily or S (50 mg) PO once daily for 4 wk (6-wk cycle). Primary and key secondary endpoints were PFS per independent review committee (IRC; RECIST v1.1) and OS in patients with PD-L1+ tumors (≥1% of immune cells) and in patients irrespective of PD-L1 expression; other secondary endpoints included OR per IRC (RECIST v1.1). **Results:** A total of 886 patients were randomized; 560 (63%) had PD-L1+ tumors. At data cut-off (Jun 2018), median follow-up was 12.0 vs 11.5 mo for A + Ax vs S groups. The table shows PFS and ORR by MSKCC and IMDC risk groups (F, favorable; I, intermediate; P, poor) and PD-L1 subgroup. Similar results for prognostic risk were seen in patients with PD-L1+ tumors. Outcome data (including PFS2) for additional clinical subgroups by baseline demographics and features will be presented. Clinical trial information: NCT02684006. **Conclusions:** A + Ax demonstrated PFS and OR benefit across all prognostic risk groups and PD-L1 subgroups vs S in aRCC.

	A + Ax (n=442)			S (n=444)		
	n (%)	Median PFS (95% CI), mo	ORR (95% CI), %	n (%)	Median PFS (95% CI), mo	ORR (95% CI), %
MSKCC risk						
F	96 (22)	NE (12.6-NE)	66 (55.2-75.0)	100 (23)	16.7 (11.1-18.6)	38 (28.5-48.3)
I	283 (64)	13.3 (8.5-NE)	50 (43.5-55.5)	293 (66)	7.9 (6.7-9.8)	24 (19.4-29.6)
P	51 (12)	5.6 (2.6-11.2)	31 (19.1-45.9)	45 (10)	2.8 (1.5-2.9)	9 (2.5-21.2)
IMDC risk						
F	94 (21)	NE (16.1-NE)	68 (57.7-77.3)	96 (22)	13.8 (11.1-18.6)	38 (27.8-48.0)
I	271 (61)	13.8 (9.7-NE)	51 (45.2-57.4)	276 (62)	8.4 (7.0-11.2)	25 (20.3-30.9)
P	72 (16)	6.0 (3.6, 8.7)	31 (20.2-42.5)	71 (16)	2.9 (2.7-5.5)	11 (5.0-21.0)
PD-L1 status						
+	270 (61)	13.8 (11.1-NE)	55 (49.0-61.2)	290 (65)	7.2 (5.7-9.7)	26 (20.6-30.9)
—	132 (30)	16.1 (9.7-NE)	47 (38.2-55.8)	120 (27)	11.1 (6.9-17.3)	28 (20.5-37.3)
Unknown	40 (9)	9.9 (7.1-NE)	40 (24.9-56.7)	34 (8)	8.4 (4.3-NE)	18 (6.8-34.5)

NE, not estimable

545 Oral Abstract Session, Sat, 2:00 PM-3:30 PM and Poster Session (Board #D6), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM

A phase II study investigating the safety and efficacy of savolitinib and durvalumab in metastatic papillary renal cancer (CALYPSO).

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Background: Metastatic papillary renal cancer (PRC) has poor outcomes and there is need for new treatments. There is a strong rationale for investigating MET and PD-L1 inhibition in this disease. In this study, we investigate savolitinib (MET inhibitor) and durvalumab (PD-L1 inhibitor) together. **Methods:** This single arm phase I/II trial explored durvalumab and savolitinib at starting doses of 1500mg Q4W and 600mg OD respectively, with a 4wk savolitinib run-in. Treatment naïve or previously treated patients with metastatic PRC were included. Response rate (RR) (RECIST v1.1) was the primary endpoint. Progression free survival (PFS), tolerability (CTCAE v4) and overall survival were secondary endpoints. Biomarkers were explored from archived tissue. **Results:** Dose escalation work identified a dose of durvalumab of 1500mg Q4W and savolitinib 600mg OD to take forward to phase II. Between Jan 2017 and Jul 2018, 42 patients were enrolled at this dose. 1 patient did not receive study treatment. The following analyses were performed on the remaining 41 patients. 12% of patients did not receive the combination (3 PD, 1 death, 1 PS deterioration). The median follow up was 8.9 months (95% CI: 6.9-10.9 months). IMDC good, intermediate and poor risk disease occurred in 29% (n=12), 63% (n=26), and 7% (n=3) patients respectively. Overall RR was 27% (11/41), while median PFS was 3.3 months (95% CI: 1.5-NR months). RR and median PFS in the previously untreated cohort (N=28) were 29% (8/28) and 12.0 months (95% CI: 1.5-NR months) respectively. Grade 3/4 toxicity occurred in 15 patients. Discontinuation for toxicity occurred in 3 patients, all due to liver toxicities. Biomarker work including PD-L1 and MET expression will be included in the analysis. **Conclusions:** The combination of savolitinib and durvalumab appears safe and associated with clinical activity in PRC. Clinical trial information: NCT02819596.

546 Oral Abstract Session, Sat, 2:00 PM-3:30 PM and Poster Session (Board #D7), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM

First-line pembrolizumab (pembro) monotherapy for advanced non-clear cell renal cell carcinoma (nccRCC): Results from KEYNOTE-427 cohort B.

David F. McDermott, Jae-Lyun Lee, Marek Ziobro, Rustem Airatovich Gafanov, Vsevolod Borisovich Matveev, Cristina Suárez, Frede Donskov, Frederic Pouliot, Boris Y. Alekseev, Pawel Wiechno, Piotr Tomczak, Miguel Angel Climent Duran, Sang Joon Shin, Rachel Kloss Silverman, Rodolfo F. Perini, Charles Schloss, Michael B. Atkins; Beth Israel Deaconess Medical Center, Boston, MA; Asan Medical Center and University of Ulsan College of Medicine, Seoul, Korea, Republic of (South); Centrum Onkologii-Instytut im. Marii Sklodowskiej, Cracow, Poland; Russian Scientific Center of Roentgenoradiology, Moscow, Russian Federation; N. N. Blokhin Cancer Research Center, Russian Academy of Medical Sciences, Moscow, Russia; Hospital General Universitari Vall d'Hebron, Barcelona, Spain; Aarhus University Hospital, Aarhus, Denmark; CHU de Quebec and Laval University, Quebec, ON, Canada; P. A. Herzen Moscow Oncology Research Institute, Ministry of Health of the Russian Federation, Moscow, Russian Federation; Maria Sklodowska-Curie Memorial Cancer Center, Warsaw, Poland; Clinical Hospital No. 1 of the Poznan University of Medical Sciences, Poznań, Poland; Instituto Valenciano de Oncología, Valencia, Spain; Yonsei University College of Medicine, Seoul, Korea, Republic of (South); Merck & Co., Inc., Kenilworth, NJ; Georgetown Lombardi Comprehensive Cancer Center, Washington, DC

Background: PD-1/L1 pathway inhibitors are effective in clear cell (cc)RCC, but efficacy of PD-1 inhibitors (or any therapy) in nccRCC has not been established. KEYNOTE-427 is a single-arm, open-label, phase 2 study of pembro monotherapy in patients (pts) with advanced ccRCC (cohort A) and nccRCC (cohort B). Cohort B results are presented. **Methods:** 165 pts with histologically confirmed nccRCC, no prior systemic therapy, measurable disease (RECIST v1.1), and KPS ≥70% enrolled. Pts received pembro 200 mg IV Q3W for 35 cycles (~2 y) or until progressive disease (PD), unacceptable toxicity, or withdrawal. Pts were followed after PD for overall survival. Primary end point: objective response rate (ORR) per RECIST v1.1 by blinded independent central review. Secondary end points included duration of response (DOR) and population description by International Metastatic RCC Database Consortium (IMDC) risk. Exploratory end points: ORR by histology and PD-L1 expression (combined positive score [CPS] ≥1 for PD-L1+). **Results:** Histology was confirmed by a central pathologist: papillary 72% (n=118), chromophobe 13% (n=21), unclassified 16% (n=26). 68% of patients were at intermediate/poor IMDC risk, and 62% were PD-L1+. At analysis, 49 pts had died and 3 had withdrawn. At a median follow-up duration of 11.1 mo (range, 0.9-21.3), 56% of pts discontinued pembro due to PD or clinical progression. Overall ORR was 24.8% (95% CI, 18.5-32.2; 8 [4.8%] CRs, 33 [20%] PRs); median DOR was not reached. ORR (95% CI) was 25.4% (17.9-34.3) with papillary, 9.5% (1.2-30.4) with chromophobe, and 34.6% (17.2-55.7) with unclassified nccRCC. ORR (95% CI) was 28.3% (16.8-42.3) with favorable and 23.2% (15.8-32.1) with intermediate/poor IMDC risk and 33.3% (24.3-43.4) and 10.3% (3.9-21.2) with CPS≥1 and CPS<1, respectively. Grade 3-5 treatment-related adverse events (TRAEs) occurred in 11% of pts; 6% discontinued due to TRAEs. 6 pts died due to AEs, 2 of which were TRAEs (pneumonia and cardiac arrest). **Conclusions:** Single-agent pembro showed encouraging antitumor activity in nccRCC, especially with papillary or unclassified histology. Safety profile of pembro was generally as expected. Clinical trial information: NCT02853344.

547 Rapid Abstract Session, Sat, 11:35 AM-12:30 PM and Poster Session (Board #D8), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM

Thirty-month follow-up of the phase III CheckMate 214 trial of first-line nivolumab + ipilimumab (N+I) or sunitinib (S) in patients (pts) with advanced renal cell carcinoma (aRCC).

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Background: N+I showed superior OS *v* S in ITT (IMDC any risk) and intermediate/poor-risk (I/P) pts with aRCC in CheckMate 214 at 17.5 mo min follow-up. **Methods:** Pts with clear cell aRCC were randomized 1:1 to N3 mg/kg + I1 mg/kg Q3W×4 and then N3 mg/kg Q2W, or S 50 mg daily for 4 wk on, 2 wk off. Co-primary endpoints were OS, RECISTv1.1 ORR and PFS per IRRC in I/P pts. PFS and ORR were assessed by investigator (inv) at 30 mo. **Results:** At 30 mo min follow-up, OS remains significantly improved in ITT and I/P pts with N+I *v* S; the HR for OS in favorable (fav) risk pts has improved for N+I *v* the previous analysis (1.22 [95% CI 0.73–2.04] *v* 1.45 [99.8% CI 0.51–4.12]). Per previous IRRC ORR (N+I, 42% [95% CI 37–47]; S, 27% [95% CI 22–31]), ORR per inv was higher with N+I *v* S in ITT and I/P pts. ORR CIs overlapped in fav pts, CR was doubled with N+I *v* S. Increasing PFS benefit with N+I *v* S is emerging in ITT and I/P pts; PFS CIs between arms remain overlapping in fav pts (Table). 15% *v* 9% of N+I and S ITT pts remain on therapy, and 48% *v* 61% have received 2nd-line systemic therapy; 39% of S pts received subsequent immune-checkpoint inhibitor therapy. Among pts who were alive with CR, 50% *v* 10% remain on treatment with N+I (n = 56) *v* S (n = 10). 5 N+I and 7 S additional pts developed Gr 3–4 drug-related AEs; 1 N+I and 3 S additional pts had AEs leading to discontinuation. No new drug-related deaths occurred. **Conclusions:** At 30 mo min follow-up, OS and ORR remain improved with N+I *v* S in ITT and I/P CheckMate 214 pts. No new safety signals emerged with longer follow-up. Clinical trial information: NCT02231749.

	ITT		I/P		Fav	
Arm; n	**N+I; 550**	**S; 546**	**N+I; 425**	**S; 422**	**N+I; 125**	**S; 124**
mOS	NR	37.9	NR	26.6	NR	NR
(95% CI), mo	(NE–NE)	(32.2–NE)	(35.6–NE)	(22.1–33.4)	(NE–NE)	(NE–NE)
HR (95% CI)	0.71 (0.59–0.86)		0.66 (0.54–0.80)		1.22 (0.73–2.04)	
***P*value**	0.0003		< 0.0001		0.443	
OS at 24 mo, %	71	61	66	53	85	88
ORR per inv	41	34	42	29	39	50
(95% CI), %	(37–46)	(30–38)	(37–47)	(25–34)	(31–48)	(41–59)
***P* value**	0.0154		0.0001		0.1436	
CR, %	11	2	11	1	8	4
mPFS per inv	9.7	9.7	8.2	8.3	13.9	19.9
(95% CI), mo	(8.1–11.1)	(8.3–11.1)	(6.9–10.0)	(7.0–8.8)	(9.9–17.9)	(15.1–23.5)
HR (95% CI)	0.85 (0.73–0.98)		0.77 (0.65–0.90)		1.23 (0.90–1.69)	
***P*value**	0.027		0.001		0.189	
PFS at 24 mo, %	31	23	30	17	35	40

NE, not estimable; NR, not reached

548 Rapid Abstract Session, Sat, 11:35 AM-12:30 PM and Poster Session (Board #D9), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM

Results of a phase II study of atezolizumab and bevacizumab in non-clear cell renal cell carcinoma (nccRCC) and clear cell renal cell carcinoma with sarcomatoid differentiation (sccRCC).

Rana R. McKay, Bradley Alexander McGregor, Kathryn Gray, John A. Steinharter, Meghara K. Walsh, David A. Braun, Abdallah Flaifel, Eliezer VanAllen, Xiao X. Wei, Sabina Signoretti, Lauren Christine Harshman, Ulka N. Vaishampayan, Toni K. Choueiri; Dana-Farber Cancer Institute, Boston, MA; Dana Farber Cancer Institute, Boston, MA; Dana-Farber Cancer Institute/ Partners CancerCare, Boston, MA; Brigham and Women's Hospital, Boston, MA; Stanford University School of Medicine, Stanford, CA; Karmanos Cancer Institute, Detroit, MI

Background: NccRCC and sccRCC have historically been underrepresented in clinical trials. Even with targeted therapy, most patients have inferior survival compared to clear cell renal cell carcinoma. The combination of atezolizumab and bevacizumab has demonstrated safety and efficacy in ccRCC. In this multicenter, phase II, open-label, single arm trial we evaluate the efficacy of atezolizumab and bevacizumab in patients with nccRCC and sccRCC with >20% sarcomatoid differentiation. **Methods:** Eligible patients had an ECOG performance status of 0-2 and may have received prior therapy. Prior PD-1/PD-L1 therapy was not allowed. Patients underwent a mandatory baseline biopsy and subsequently received atezolizumab 120 mg and bevacizumab 15 mg/kg intravenously every 3 weeks. Patients remained on therapy until radiographic progression, unacceptable adverse events, or withdrawal. The primary end point was overall response rate (ORR) as determined by RECIST version 1.1. **Results:** 65 patients were enrolled of whom 52 had ≥1 response assessment and were included in this analysis. 36 patients had nccRCC (papillary n=14, chromophobe n=8, unclassified RCC n=3, collecting duct n=3, translocation n=3, other n=5), and 16 patients had sccRCC. 17 patients received prior systemic therapy, 16 of whom had nccRCC. The ORR was 31% in the overall cohort (Table 1). 10 patients (19%) developed grade 3 treatment-related adverse events (AEs), half of which were immune-related. There were no grade 4-5 AEs. **Conclusions:** In this study, we show that therapy with atezolizumab and bevacizumab was safe and demonstrated anti-tumor activity in nccRCC and sccRCC. Further analyses will report ORR by histologic subtype and PD-L1 expression status. Analysis of tissue and blood-based biomarkers of response are ongoing. Clinical trial information: NCT02724878.

Table 1.

			Histology		Prior Systemic Therapy	
		Total N=52	sccRCC N=16	nccRCC N=36	No N=35	Yes N=17
ORR	N (%)	16 (31)	7 (44)	9 (25)	8 (23)	8 (47)
Stable Disease	N (%)	23 (44)	5 (31)	18 (50)	18 (51)	5 (29)

549 Rapid Abstract Session, Sat, 11:35 AM-12:30 PM and Poster Session (Board #D10), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM

CB-839, a glutaminase inhibitor, in combination with cabozantinib in patients with clear cell and papillary metastatic renal cell cancer (mRCC): Results of a phase I study.

Funda Meric-Bernstam, Richard J. Lee, Bradley Curtis Carthon, Othon Iliopoulos, James Walter Mier, Manish R. Patel, Nizar M. Tannir, Taofeek Kunle Owonikoko, Naomi B. Haas, Martin Henner Voss, James J. Harding, Ramaprasad Srinivasan, Geoffrey Shapiro, Melinda L. Telli, Pamela N. Munster, Richard D. Carvajal, Yonchu Jenkins, Sam H. Whiting, Johanna C. Bendell, Todd Michael Bauer; University of Texas MD Anderson Cancer Center, Houston, TX; Massachusetts General Hospital Cancer Center, Boston, MA; Emory University Winship Cancer Institute, Atlanta, GA; Harvard Medical School, Charlestown, MA; Beth Israel Deaconess Medical Center, Dana-Farber/Harvard Cancer Center, Boston, MA; Florida Cancer Specialists/Sarah Cannon Research Institute, Sarasota, FL; The University of Texas MD Anderson Cancer Center, Houston, TX; Emory University, Atlanta, GA; Penn Medicine Abramson Cancer Center, Philadelphia, PA; Memorial Sloan Kettering Cancer Center, New York, NY; Memorial Sloan Kettering Cancer Center and Weill Cornell Medical College, New York, NY; National Cancer Institute at the National Institutes of Health, Bethesda, MD; Dana-Farber Cancer Institute, Boston, MA; Stanford University School of Medicine, Stanford, CA; University of California San Francisco, San Francisco, CA; Columbia University Medical Center, New York, NY; Calithera Biosciences, Inc., South San Francisco, CA; Gradalis Inc., Dallas, CA; Sarah Cannon Research Institute/Tennessee Oncology, Nashville, TN

Background: Glutaminase (GLS) is a key enzyme that controls glutamine utilization, a metabolic pathway upregulated in RCC and important for tumor proliferation and survival. CB-839 is a first-in-clinic, small molecule, reversible, oral GLS inhibitor that synergizes with cabozantinib (Cabo), a VEGFR2/MET/AXL inhibitor, in preclinical RCC models to inhibit metabolic pathways and enhance anti-tumor activity. Cabo monotherapy is associated with a 17% overall response rate (ORR) for clear cell (cc) mRCC (Choueiri et al. Lancet Oncol. 2016). Here we present findings from a Phase 1 study cohort evaluating the safety, efficacy, and recommended Phase 2 dose (RP2D) of CB-839 + Cabo in patients (pts) with mRCC as 2L+ therapy. **Methods:** Eligible pts had mRCC with cc or papillary histology, ECOG 0-1, RECIST measurable disease, and, for cc pts, treatment with ≥1 prior anti-VEGF therapy. Escalating doses of CB-839 (600-800 mg PO BID) plus Cabo (60 mg PO QD) were evaluated using a 3+3 design. Tumor response was assessed per RECIST 1.1 every 8 wks. **Results:** The CB-Cabo cohort enrolled 13 pts with a median 3 (range, 0-7) prior lines of therapy. No maximum tolerated dose was reached; 800 mg was selected as the CB-839 RP2D. The most common treatment-related AEs (occurring in >25% of pts) were diarrhea (62%), decreased appetite (46%), ALT increased (39%), fatigue (39%), AST increased (31%), nausea (31%), and rash (31%); Gr ≥3 treatment-related AEs included diarrhea, hypertension, platelet count decreased, and hallucination (n=1 each). Among 12 evaluable pts, ORR was 42% and disease control rate (DCR = complete response + partial response [PR] + stable disease [SD]) was 100%: 42% (5/12) PR, 58% (7/12) SD. Among 10 evaluable cc mRCC pts, 50% (5/10) had PRs, 50% (5/10) SDs. As of Sept 24, 2018, 5 pts received >12 months treatment; 4 remain on study. **Conclusions:** CB-839 plus Cabo showed encouraging clinical activity and tolerability in heavily pretreated mRCC pts, with response rates for cc mRCC (50% ORR, 100% DCR) comparing favorably to historical Cabo monotherapy. A randomized Phase 2 study of CB-839 + Cabo vs. Cabo + placebo in cc mRCC is ongoing. (CANTATA; NCT0342821) Clinical trial information: NCT02071862.

550 Rapid Abstract Session, Sat, 11:35 AM-12:30 PM and Poster Session (Board #D11), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM

Analysis of overall survival (OS) based on early tumor shrinkage in the phase III METEOR study of cabozantinib (cabo) versus everolimus (eve) in advanced renal cell carcinoma (RCC).

Ignacio Duran, Pablo Maroto, Cristina Suárez, Daniel E. Castellano, Xavier Garcia del Muro, Luis Costa, Lidia Martin-Couce, Fawzi Benzaghou, Stephane Thomas, David W. Markby, Toni K. Choueiri; Department of Medical Oncology, Hospital Universitario Marqués de Valdecilla, Santander, Spain; Department of Medical Oncology, Hospital de la Santa Creu i Sant Pau, Barcelona, Spain; 3.Vall d'Hebron University Hospital and Institute of Oncology, Universitat Autonoma de Barcelona, Barcelona, Spain; Hospital Universitario 12 de Octubre, I + 12 Research Institute, Madrid, Spain; Medical Oncology Department, Institut Catalá d'Oncologia, IDIBELL, L'Hospitalet de Llobregat, Barcelona, Spain; Centro Hospitalar de Lisboa Norte, Instituto de Medicina Molecular, Faculdade de Medicina, Universidade de Lisboa, Lisbon, Portugal; Ipsen Pharma, Barcelona, Spain; Ipsen Innovation, Les Ulis, France; Exelixis, Inc., Alameda, CA; Department of Medical Oncology, Lank Center for Genitourinary Oncology, Dana-Farber Cancer Institute, Boston, MA

Background: In the phase 3 METEOR study (NCT01865747), cabo improved OS (median 21.4 vs 16.5 mo; HR, 0.66; 95% CI, 0.53–0.83), progression-free survival and objective response rate compared with eve in patients (pts) with previously treated advanced RCC (Choueiri 2016). Retrospective studies have shown that early tumour shrinkage (eTS), based on target lesion reduction from baseline to first post-baseline scan, has predictive value for targeted therapies in RCC (Grunwald 2015; Grunwald 2016); here we evaluate its impact on OS in METEOR. **Methods:** In total, 658 pts were randomized 1:1 to receive cabo (60 mg qd) or eve (10 mg qd), stratified by MSKCC risk group and number of prior VEGFR TKIs. Target lesion size was assessed by independent radiology review using CT/MRI scans at baseline, every 8 wk for the first 12 mo and every 12 wk thereafter. Median OS was estimated for pts with ≥30% eTS, any eTS or no eTS at first post-baseline scan (week 8); data cutoff, 2 October 2016 (Motzer 2018). **Results:** Median follow-up was 28 mo (IQR 25, 30). Median (range) time to objective response was 1.91 (1.6, 11.0) mo with cabo and 2.14 (1.9, 9.2) mo with eve, and corresponded to the time to the first post-baseline scan. A greater proportion of pts had ≥30% eTS with cabo (20%) than with eve (5%) and the rate of any eTS was higher in the cabo arm (73%) than with eve (47%; Table). Median OS with cabo vs eve for pts with ≥30% eTS was not reached (NR; 95% CI, 23.7–NR) vs 10.2 mo (95% CI, 3.9–NE), respectively (stratified HR, 0.45; 95% CI, 0.21–0.95; $p<0.05$). Median OS with cabo vs eve for pts with any eTS was 23.7 (95% CI, 21.7–27.7) vs 17.3 mo (95% CI, 15.4–20.8), respectively; (stratified HR, 0.62; 95% CI, 0.48–0.80; $p<0.05$). OS was similar for cabo and eve for pts with no eTS. **Conclusions:** Cabo demonstrated a higher rate and greater magnitude of eTS at first post-baseline scan compared with eve, and eTS was associated with prolonged OS in pts treated with cabo. Clinical trial information: NCT01865747.

Proportion of pts in each subgroup.

Early tumor shrinkage[a]	Cabo, n (%) (N=330)	Eve, n (%) (N=328)
≥30%	65 (19.7)	16 (4.9)
Any	242 (73.3)	155 (47.3)
None	77 (23.3)	156 (47.6)
Unknown	11 (3.3)	17 (5.2)

[a]From baseline to first post-baseline scan (week 8)

551 Rapid Abstract Session, Sat, 11:35 AM-12:30 PM and Poster Session (Board #D12), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM

Alterations in DNA damage repair (DDR) genes and outcomes to systemic therapy in 225 immune-oncology (IO) versus tyrosine kinase inhibitor (TKI) treated metastatic clear cell renal cell carcinoma (mccRCC) patients (pts).

Yasser Ged, Joshua Chaim, Andrea Knezevic, Maria Isabel Carlo, Ashley Foster, Darren R. Feldman, Min Yuen Teo, Nadeem Riaz, Chung-Han Lee, Sujata Patil, Timothy An-thy Chan, A. Ari Hakimi, Robert J. Motzer, Martin Henner Voss; Memorial Sloan Kettering Cancer Center, New York, NY

Background: Loss of function alterations in DDR genes including core components of mismatch repair and homologous recombination deficiency pathways are associated with tumorigenesis and may determine benefit from IO therapies as shown in colon cancer. The significance for standard IO and TKI treatments in mccRCC is unknown. **Methods:** Genomic data and treatment outcomes were retrospectively collected for two large cohorts of mccRCC: pts treated with pure IO therapy (cohort 1); and pts receiving first-line TKI (cohort 2). Tumor and germline DNA was subject to targeted panel testing across >400 genes of interest, including 34 DDR machinery genes. Presence of truncating mutations, deletions and functionally validated missense mutations identified individual patient as 'DDR altered' (DDRa). Tumor mutational burden (TMB) was inferred for all pts. Non-parametric tests were applied to determine association between DDR status, TMB and treatment outcomes. **Results:** 225 pts were included (cohort 1=107, cohort 2=118), 37 (16%) were DDRa. Most commonly altered genes were *ATM* (n=8, 4%) and *CHEK2* (n=8, 4%). DDR germline alterations were seen in 12 pts (5%). Median TMB was 4.1 per megabase (range: 0-21.7), and higher TMB (≥ median) was associated with being DDRa (Fisher's exact, p=0.03). DDRa status correlated significantly with longer overall survival (OS) in the IO cohort (HR 0.29, logrank p=0.04) but not in the TKI cohort (HR 0.74, logrank p=0.44). We found no interaction between objective response and DDR status in either cohort. **Conclusions:** Loss of function in DDR genes was associated with superior OS in IO-treated but not in TKI-treated RCC pts. Possible underlying mechanisms beyond increase in TMB observed here deserve further study.

Cohort 1 (IO)	IO: All pts (n=107)	IO: DDR wild type (n=90)	IO: DDRa (n=17)	
Median OS	50.0	39.4	Not reached	Logrank
months	CI: 32.6-NE	CI: 26.7-NE	CI: NE-NE	HR 0.29, (0.09-0.95) p=0.04
Cohort 2 (TKI)	**TKI: All pts (n=118)**	**TKI: DDR wild type (n=98)**	**TKI: DDRa (n=20)**	
Median OS	55.7	52.5	72.9	Logrank
months	CI: 41.1-97.6	CI: 40.0-115.1	CI: 38.5-NE	HR 0.73, (0.33-1.62) p=0.44

NE=Not estimated

552 Poster Session (Board #D13), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM

Novel predictive models of early death less than one year in patients with metastatic RCC treated with first-line tyrosine kinase inhibitors.

Minyong Kang, Jae Young Joung, Tae Jin Kim, Hwang Gyun Jeon, Byong Chang Jeong, Seong Il Seo, Seong Soo Jeon, Hyun Moo Lee, Hyun Hwan Sung; Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea, Republic of (South); National Cancer Center, Goyang, Korea, Republic of (South); Samsung Medical Center, Seoul, Korea, Republic of (South)

Background: Although the IMDC model can provide useful information on overall survival outcomes in patients with metastatic renal cell carcinoma (mRCC), this model maybe invaluable in patients who experience early death less than one year after initial systemic therapy. Here, we aimed to develop a new prognostic model which can predict early death in patients with mRCC receiving first line tyrosine kinase inhibitors (TKI). **Methods:** We retrospectively evaluated a total of 498 patients treated with first line line TKI among 537 patients with mRCC at our institution. The primary endpoint was the rate of early death within 1 year after first line TKI administration. We selected statistically significant factors predicting early death by performing multiple logistic regression. Modified IMDC model 1 based on existing IMDC model and model 2 composed of new variables were generated. The prediction accuracy was evaluated by calculating the concordance index (C-index). Area under curve (AUC) and net reclassification index (NRI) using ROC curve analysis were used to compare the predictive power between the models. **Results:** Overall mortality was 59.0% (n = 294) in 498 patients, and early mortality was 19.7% (n = 98) within 1 year after first line TKI administration. The C-index of the IMDC model for early death was 0.655. Five variables were selected: previous nephrectomy, BMI, multiple metastases, previous metastasectomy and serum albumin level. The C-index of the model 1, which includes five new variables plus variables in the IDMC model, is 0.823, showing a significant improvement over the IDMC model. In model 2, hemoglobin and neutrophil levels were added in new five variables, and the C-index was 0.822. For the IMDC model, there was a significant NRI difference in both models 1 and 2, but no significant difference in NRI between models 1 and 2. (-0.0368 [95% CI = -0.1416 - 0.0681]; p = 0.491). **Conclusions:** In this study, we suggest modified IMDC models for predicting 'early death less than one year in patients with mRCC treated with first line TKI. These novel models can provide better treatment strategies and counseling in patients with mRCC who were treated by first line TKI.

553 Poster Session (Board #D14), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM

Genomic analysis of mitochondrial mutations in chromophobe renal cell carcinoma by using low-depth whole genome sequencing.

Minyong Kang, Yong Ho Shin, Jae Young Joung, Seong Il Seo; Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea, Republic of (South); National Cancer Center, Goyang, Korea, Republic of (South)

Background: Mitochondria have a circular genome that is independent of the nuclear genome of the nucleus. Mutations of mitochondrial DNA rarely occur during tumorigenesis. Chromophobe renal cell carcinoma (chRCCC) is a type of kidney tumor characterized by a morphologic abnormality of mitochondria. However, there is still little research on the existence of mitochondrial mutation in chRCC and how it plays a role in tumorigenesis. Here, we investigated the mutation patterns of mitochondria genome in chRCC using low-depth sequencing technique. **Methods:** We evaluated 17 patients with chRCC who underwent radical nephrectomy from December 2010 to January 2017. Mitochondrial genomic analysis was performed by low-depth sequencing. Varscan and MToolBox analysis programs were used to search for mutations. Germline mutation information reported in MtDB, Phylotree, and Mitomap databases was used to allocate patient haplogroups and exclude germline mutations. **Results:** Whole genome sequencing of 17 chRCC tissues at an average depth of 1x based on whole genome revealed that the mitochondrial genome was sequenced to an average of 630x. A total of 1,206 Haplotype frequency $>$ 0.25 mutations were found, of which 30 were mutations not reported in the database. Seven of them were identified as synonymous mutations (average of 0.41 and 41% per tumor), and three were truncating mutations (average of 0.18 per tumor; 18%). Truncating mutations were specifically identified as two frameshift indel and one stop gain mutation. **Conclusions:** In summary, our study showed that the frequency of truncating mutation of mitochondrial DNA was higher in chRCC compared to other solid tumors which have a low frequency of 1-2%. This finding suggests that dysfunctional mitochondria may play an oncogenic role in tumorigenesis of chRCC, while other tumors are predicted to undergo negative selection of mitochondrial truncating mutations during tumorigenesis. Based on these results, we are performing prospective study for evaluating mutational characteristics and associated morphological changes of mitochondria under electron microscopy.

554 Poster Session (Board #D15), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM

Thick perirenal fat predicts the growth pattern of renal cell carcinoma.

Eiji Kashiwagi, Kenjiro Imada, Masaki Shiota, Ario Takeuchi, Junichi Inokuchi, Katsunori Tatsugami, Masatoshi Eto; Kyushu University Graduate School of Medical Sciences, Fukuoka, Japan

Background: Partial nephrectomy is the standard surgical treatment for T1a renal cell carcinoma (RCC) and select T1b. Among these tumor classes, the tumor location can be divided into inner or outer. However, little attention has been paid to the mechanism of the pattern of RCC growth. In our body, there are two types of adipose tissue: white adipose tissue (WAT) and brown adipose tissue (BAT). WAT is important for energy storage and BAT is important for thermogenesis. BAT expresses uncoupling protein 1 (UCP-1), and mainly located in mediastinal, supraclavicular and perirenal tissues. But no studies have been done to investigate the relationship between RCC and BAT.In this study, we examined the association between adipose tissue, especially around kidney, and the growth pattern of RCC. **Methods:** We retrospectively reviewed computed tomography scans of 153 patients with stage 1 RCC who underwent radical or partial nephrectomy in our hospital between January 2013 and July 2016. We calculated the visceral/subcutaneous/perirenal fat volumes using SYNAPSE VINCENT. Of the 60 patients, the perirenal fat was immunohistochemically stained for leptin, adiponectin, COX-2 and UCP-1, and the association with outward tumor protrusion was evaluated. **Results:** Of the 153 cases, 88 had confirmed outward expansion (57.5%), 110 were classed as pT1a (52 and 58 with outer and inner expansion, respectively), 43 were classed as pT1b (36 and 7 with outer and inner expansion, respectively; $P < 0.0001$). Multivariate Cox model showed a trend toward significance in pT1b (vs. pT1a, OR 6.033, 95% CI = 2.409-15.108, P = 0.0001), perirenal fat percentage > 1.0 (vs. ≤ 1.0, OR 2.596, 95% CI = 1.205-5.591, P = 0.014). as independent predictors for outer protrusion. Immunohistochemical staining was positive for UCP-1 expression in 31 out of 41 outgrowth types (75.6%), and all 19 endogenous types (100%; $P = 0.003$). **Conclusions:** Renal cell carcinoma with thick perirenal fat correlates with an increased likelihood of developing outward tumor protrusion; therefore, fat distribution and UCP1 expression may affect the development of renal cell carcinoma.

555 Poster Session (Board #D16), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM

Axitinib versus sunitinib as first-line therapies for metastatic renal cell carcinoma: A multicenter retrospective analysis.

Shingo Hatakeyama, Toshiaki Tanaka, Yoshinori Ikehata, Naoki Fujita, Naoya Masumori, Hiroshi Kitamura, Takahiro Yoneyama, Yasuhiro Hashimoto, Chikara Ohyama; Hirosaki University Graduate School of Medicine, Hirosaki, Japan; Department of Urology, Sapporo Medical University School of Medicine, Sapporo, Japan; Oji General Hospital, Tomakomai, Japan; Department of Urology, Hirosaki University Graduate School of Medicine, Hirosaki, Japan; Sapporo Medical University, Chuo-Ku, Japan

Background: No previous study has compared the efficacy and safety of first-line axitinib and sunitinib. We aimed to compare oncological outcomes and safety of axitinib and sunitinib in patients with treatment-naïve metastatic renal cell carcinoma (mRCC). **Methods:** We retrospectively evaluated 169 patients with mRCC who were treated with axitinib or sunitinib as the first-line therapy in five hospitals between October 2008 and August 2018.Oncological outcomes and safety were compared between axitinib (n = 68) and sunitinib (n = 101) groups. Inverse probability of treatment weighted (IPTW)-adjusted Cox regression analysis was performed to evaluate effects of first-line therapies on progression-free survival (PFS), cancer-specific survival (CSS), and overall survival (OS). **Results:** Patients in the axitinib group were significantly older (66 vs 72 years) than those in the sunitinib group. Median relative dose intensity was significantly higher in the axitinib group (94 $\pm$ 62%) than in the sunitinib group (65 $\pm$ 20%; P = 0.001). Objective response rate was significantly higher in the axitinib group (21%) than in the sunitinib group (10%; P = 0.042). IPTW-adjusted Cox regression analysis revealed significant differences in CSS and OS but not in PFS between the two groups. Safety in terms of grade $\geq$3 adverse events was significantly different between the axitinib (34%) and sunitinib (55%) groups (P = 0.006). **Conclusions:** Compared with sunitinib, axitinib significantly prolonged CSS and OS and showed a safer profile as the first-line therapy for treatment-naïve mRCC.

556 Poster Session (Board #D17), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM

Impact of disagreement between the IMDC and MSKCC risk groups on prognosis in patients with metastatic renal cell carcinoma.

Shingo Hatakeyama, Toshiaki Tanaka, Yoshinori Ikehata, Naoki Fujita, Hayato Yamamoto, Takahiro Yoneyama, Yasuhiro Hashimoto, Naoya Masumori, Hiroshi Kitamura, Chikara Ohyama; Hirosaki University Graduate School of Medicine, Hirosaki, Japan; Department of Urology, Sapporo Medical University School of Medicine, Sapporo, Japan; Oji General Hospital, Tomakomai, Japan; Department of Urology, Hirosaki University Graduate School of Medicine, Hirosaki, Japan; Sapporo Medical University, Chuo-Ku, Japan

Background: As the clinical implication of the risk group disagreement between the risk models remains unclear, we aimed to investigate the impact of the risk group disagreement between the Memorial Sloan Kettering Cancer Center (MSKCC) and the International Metastatic Renal Cell Carcinoma Database Consortium (IMDC) models on prognosis. **Methods:** We retrospectively evaluated 176 patients with metastatic renal cell carcinoma (mRCC) who were treated with tyrosine kinase inhibitors as first-line therapy in five hospitals between October 2008 and August 2018. The risk group classification differences between the MSKCC and the IMDC models were evaluated using criteria of agreement (identical risk group in both the MSKCC and IMDC models) and disagreement (not identical risk group in both the MSKCC and IMDC models). The agreement of risk stratification between the MSKCC and IMDC models was evaluated using Cohen's k coefficient. Oncological outcomes were compared between the agreement and disagreement groups. **Results:** The number of patients with agreement, upgrade, and downgrade was 135/176 (77%), 39/176 (22%), and 2/176 (1.1%), respectively. Of 41 patients with disagreement, reclassification from the MSKCC-intermediate to the IMDC-poor-risk group was most frequent (n = 34/176, 19%). The Cohen's k coefficient for agreement of the two risk models was substantial with k value of 0.613 ($P < 0.001$). Significantly poorer prognosis was observed in patients with disagreement than in those with agreement. **Conclusions:** Disagreement between the MSKCC and IMDC models may have a negative impact on prognosis in patients with mRCC. Further study is necessary to validate our findings.

557 **Poster Session (Board #D18), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM**

Modeling of prognostication and differential genomic expression in the tumor microenvironment of clear cell renal cell carcinoma.

Sunyoung S. Lee, Seok Joon Kwon, Dong Eun Lee, Seongwon Lee, Andrew Baird, Shinyoung Park, Jillian Dolan, Saby George; Roswell Park Comprehensive Cancer Center, Buffalo, NY; Korea Institute of Science and Technology, Seoul, Korea, Republic of (South); Brighton and Sussex Medical School, Brighton, United Kingdom; National Institute for Mathematical Sciences, Daejeon, Korea, Republic of (South); University of Pittsburgh, Pittsburgh, NY; University at Buffalo School of Medicine, Buffalo, NY

Background: Stroma in the tumor microenvironment (TME) influences prognosis and response to therapy. Few mathematical models exist to prognosticate patients (pts), based on mRNA expressivity in the TME. **Methods:** Clinical outcomes data and mRNA-seq of 533 pts with clear cell renal cancer were obtained from TCGA. Expressivity of 191 genes enriched in cellular and structural elements of TME and clinical data were analyzed via machine learning, multivariate nonlinear regression with confined optimization, and Kaplan-Meier (KM) analysis. **Results:** Prognostication was modeled with higher risk score (RS) representing worse prognosis in each stage (Table). P/G is the ratio of genes associated with poor (61 genes) to good (14) prognosis (refer to presentation). Based on RS, pts in each stage were clustered into 2 groups (high and low RS), showing 2 KM curves with $p < 0.001$ in each stage. Analysis of immune profiles in these 2 groups shows that in stage 1, expression of genes related to immune activation (IA) is not statistically different in high and low RS groups, but expression of genes related to immune inhibition (II) is higher in high RS group. In high RS groups of stage 2-4, IA genes are highly co-expressed with II genes. In high RS groups of all stages, expression of both IA and II genes increases as stage increases. In low RS groups, IA genes increase as stage increases, but II genes do not. **Conclusions:** Machine learning and mathematical modeling of RS and gene analysis show that IA genes are suppressed by high degree of II in high RS groups of advanced stages, contributing to worse prognosis. RS enables prognostication of pts encountered in the clinic, given genomic profiles.

Stage	RS
1	$0.1648 + 3.4137 \times \mathbf{Age}^{-2.5173} + 0.4574 \times \mathbf{P/G}^{0.2057}$
2	$-4.8127 + 2.4426 \times \mathbf{Age}^{0.0695} + 2.1741 \times \mathbf{P/G}^{0.0407}$
3	$-0.0397 - 0.1084 \times \mathbf{Age}^{-2.0579} + 0.7196 \times \mathbf{P/G}^{0.1529}$
4	$0.7157 + 2.8591 \times \mathbf{Age}^{-1.9610} + 0.0177 \times \mathbf{P/G}^{3.0892}$

IA gene groups: cytotoxic T, B, NK, T-helper 1 cells, IFN, cytolytic activity, T cell co-stimulation, antigen presentation II gene groups: regulatory T cells, desmoplasia, immunosuppressive chemokines, immune checkpoints, angiogenesis, cancer stem cells, epithelial-mesenchymal transition, neutrophils

558 Poster Session (Board #D19), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM

Results from a phase I expansion cohort of the first-in-class oral HIF-2α inhibitor PT2385 in combination with nivolumab in patients with previously treated advanced RCC.

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Background: The transcription factor hypoxia-inducible factor (HIF)-2α has been established as an oncogenic driver in clear cell renal cell carcinoma (ccRCC) due to underlying *VHL* deficiency. Activation of HIF-2α can also promote immunosuppression. In preclinical models, HIF-2α inhibition demonstrated increased efficacy in combination with checkpoint inhibitors (Han et al. AACR 2016). In a Phase 1 dose escalation/expansion trial in heavily pre-treated advanced ccRCC patients, PT2385 monotherapy was associated with variability in drug exposure with higher therapeutic exposure associated with improved anti-tumor activity (Courtney et al. JCO 2018). **Methods:** In the current Phase 1 expansion cohort, patients with advanced ccRCC who had received 1-3 prior therapies (including at least one VEGF(R)-targeting agent) were treated with PT2385 (800 mg PO BID) in combination with nivolumab (3 mg/kg IV Q2Weeks) to evaluate safety, efficacy, and pharmacokinetics. **Results:** 50 patients were enrolled. Median age was 62 with 58% ECOG 1 and 42% ECOG 2. Median number of prior therapies was 1; 42% of patients received ≥2 prior lines of therapy. The most common all-grade AEs were anemia (46%), fatigue (46%), nausea (36%), and arthralgia (30%). The most common Grade 3 AE's were anemia (4%), fatigue (4%), and hypoxia (4%). Two Grade 4 events of elevated ALT and increased lipase/amylase were observed. As of August 31, 2018, ORR = 22% (1 CR, 10 PR). At a median follow up of 12.4 months (m), median PFS was 7.3 m for all patients. Patients who had sub-therapeutic exposures (< 300 ng/ml) of PT2385 (n = 17) had a median PFS of 4.7 m compared to patients with therapeutic exposures of PT2385 (n = 33), who had a median PFS of 10.0 m. **Conclusions:** The combination of PT2385 + nivolumab was well tolerated and demonstrated promising anti-tumor activity in advanced ccRCC patients, most notably in patients who achieved therapeutic exposure of PT2385. Single agent and combination studies with PT2977, a second-generation HIF-2α inhibitor with an improved PK profile, are ongoing. Clinical trial information: NCT02293980.

559 Poster Session (Board #D20), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM

Treatment utilization trends and outcomes in renal liposarcoma (RLS): A National Cancer Database (NCDB) analysis.

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Background: RLS is an extremely rare neoplasm with only few case reports documented in the literature. Due to the rarity of this disease, level 1 evidence guiding optimal patient management is lacking. Utilizing the NCDB, we analyzed the current treatment patterns and outcomes in patients with RLS in the United States. **Methods:** The NCDB was queried from 2004- 2015 for patients diagnosed with T1-4N0-1M0 RLS. Baseline patient characteristics were summarized using descriptive statistics. Impact of baseline demographic, clinicopathologic variables and treatment on overall survival (OS) was evaluated using univariate (UV) and multivariable (MV) cox proportional hazards analysis. **Results:** 136 patients diagnosed with non-metastatic RLS between 2004- 2015 were included in this analysis. Median age at diagnosis was 64.7 years. Males and females had equal preponderance (50% each). 89% (n = 121) were Caucasian, while only 6% were African American. T staging was based on AJCC 8th edition. 20% of patients had T1 disease, 17% had T2, while T3 and T4 stage was present in 26% and 37% of cases respectively. Only 7% (n = 10) had lymph node (LN) involvement. Dedifferentiated RLS was the most common histology (44%). 59% (n = 80) had radical nephrectomy, 12% (n = 17) had partial nephrectomy, and 17% had nephrectomy NOS. Adjuvant radiation and chemotherapy were used in 15% (n = 20) and 3.6% (n = 5) of patients respectively. Median OS was 41 months (20-76 mos). On UV analysis age $\leq$ 70 years and sex had a statistically significant effect on OS (HR: 0.387 and 0.549, $p < 0.001$ and 0.04 respectively). On MV analysis adjusting for age and sex, female patients had a significantly improved OS compared to males (47 vs 36.7mos, HR-0.45, CI: 0.250-0.804 $p < 0.05$). **Conclusions:** RLS is a rare and aggressive malignancy with poor outcomes even at localized stage. Age at diagnosis and sex had a statistically significant impact on OS. Given the lack of prospective data, our study provides insights into the prognosis of this rare disease. Additional studies are needed to better guide the optimal management of this rare disease.

560 Poster Session (Board #D21), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM

Sporadic angiomyolipomas (AMLs) growth kinetics while on everolimus (SAGE).

Daniel M. Geynisman, Brian T. Kadow, Brian M. Shuch, Stephen A. Boorjian, Surena F. Matin, Edward Rampersaud, Daniel McClean, Barton N Milestone, Elizabeth R. Plimack, Matthew R. Zibelman, Alexander Kutikov, Marc C. Smaldone, David Chen, Rosalia Viterbo, Shreyas Joshi, Richard E. Greenberg, Lois Malizzia, Thomas McGowan, Eric A. Ross, Robert Uzzo; Fox Chase Cancer Center, Philadelphia, PA; Yale School of Medicine, New Haven, CT; Mayo Clinic, Rochester, MN; The University of Texas MD Anderson Cancer Center, Houston, TX; Duke University, Durham, NC; Fox Chase Cancer Center, Temple Health, Philadelphia, PA

Background: Level I evidence exists demonstrating the efficacy of the mTOR inhibitor everolimus (EVE) in decreasing tumor volume of syndromic angiomyolipomas (AMLs) among patients with Tuberous Sclerosis. No prospective data are available regarding the effect of mTOR inhibition on growth kinetics in patients with sporadic AMLs. **Methods:** We conducted a multi-institutional, prospective, phase 2 trial with an optimal two-stage Simon design in patients presenting with $>$ 3cm sporadic AMLs who were candidates for surgical or percutaneous intervention. Response was defined as $\geq$25% volumetric reduction of the AML. Planned enrollment was 43 patients to test the null hypothesis at a 5% level of significance with 80% power. Baseline, 4- and 6-month volumetric analysis was performed by dynamic contrast-enhanced MRI (DCE-MRI). Patients received EVE 10mg for four 28-day cycles, at which point EVE was discontinued in those with $<$ 25% volumetric reduction. Those with $\geq$ 25% volumetric reduction received two additional cycles of EVE. Dose reductions and interruptions were allowed to 5 mg QOD. Conservative stopping rules were established for toxicity, given the benign nature of AMLs. **Results:** The early stopping rules for both efficacy and toxicity were invoked. We enrolled 20 patients (median age = 68) from 5 centers with 21 sporadic AMLs. 11/20 (55%) patients completed 4 cycles of EVE, while 7/20 (35%) completed 6 cycles. Median days on treatment was 88 (2 cycles). 4/20 (20%) patients were withdrawn due to toxicity, while 8/20 (40%) withdrew due to personal preference. Dose reductions were required in 6/20 (30%) patients, and 5/20 (25%) patients had grade 3 toxicities which resolved upon discontinuation or dose reduction of EVE. At 4-month MRI, 10/16 (62.5%) patients had a $\geq$25% reduction in volume (mean = 54.1% decrease). At 6-month MRI, 8/12 (66.6%) patients had a $\geq$25% reduction in volume (mean = 51.5% decrease). **Conclusions:** EVE was effective in reducing tumor volume in patients with sporadic AMLs but was associated with a high rate of treatment termination due to patient preference or prespecified AEs. Neoadjuvant EVE may be useful in potentiating surgical resection of large or anatomically complex AMLs. Clinical trial information: NCT02539459.

561 Poster Session (Board #D22), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM

A phase I/II trial of pazopanib alternating with bevacizumab in treatment-naïve metastatic clear cell renal cell carcinoma (CCRCC) patients: Phase I results.

Saby George, Laurie Herbst, Marcus Sikorski, Ann Marie Diraddo, Gissou Azabdaftari, Charles Roche, Eric Kauffman, Qiang Li, Thomas Schwaab, Ellis Glenn Levine, Roberto Pili, Gurkamal S. Chatta, Leonard Joseph Appleman, Adrienne Groman, Rahul Atul Parikh, Alan Hutson; Roswell Park Comprehensive Cancer Center, Buffalo, NY; Roswell Park Cancer Institute, Buffalo, NY; Indiana University School of Medicine, Indianapolis, IN; Virginia Mason Medical Center, Seattle, WA; University of Pittsburgh Medical Center, Pittsburgh, PA; University of Kansas Cancer Center, Westwood, KS

Background: Pazopanib as single agent and bevacizumab plus interferon were approved for use in metastatic RCC (MRCC) based on their ability to modulate the vasculature and prolong progression free survival. VEGF levels rose unopposed while using VEGF tyrosine kinase inhibitors (TKI) without break. We hypothesized that adding a break as well as bevacizumab which removes VEGF could prolong PFS in MRCC pts. **Methods:** This phase I trial was conducted in VEGF treatment naïve MRCC pts. This trial utilized a unique regimen of alternating Pazopanib (day 1-28) with bevacizumab (on days 36 and 50) in a 10-week cycle. The study employed a classic 3+3 design for dose escalation (dose levels in table 1). Safety utilized CTCAE version 4.0 and response evaluation was done using RECIST 1.1 criteria. The primary endpoint of this phase I trial was to find the recommended phase 2 dose (RP2D) of this novel regimen. Key secondary endpoints included objective response rate (ORR), safety/ toxicity and pharmacokinetics. Phase I safety committee acknowledged the completion and approved reporting of Phase I portion of this study. **Results:** This phase I study was conducted at two academic centers. Twenty-five pts were enrolled in the phase I portion. Median age was 64 years and 68% were male patients. The Commonest adverse events (AE) included fatigue (64%), diarrhea (52%), hypertension (48%), nausea (36%), dysgeusia (36%), vomiting (24%) and proteinuria (28%). The commonest grade 3/4 AE of more than 5% frequency included hypertension (20%) and proteinuria (12%). The dose levels 1 and 4 were expanded due to one DLT each and RP2D was established at dose level 4. The ORR was 25% among evaluable pts who completed at least one cycle of therapy (n=20). The median PFS of the ITT cohort (n=25) was 20.9 months. **Conclusions:** These data demonstrate that this novel regimen could be safely tested in a phase II trial. The safety and efficacy data suggest that this novel regimen could be optimal for MRCC patients with favorable/intermediate risk. Clinical trial information: NCT01684397.

Dose Level	Pazopanib Days 1 - 28	Bevacizumab Day 36 and Day 50
-1	400 mg daily	5 mg/kg
1	600 mg daily	5 mg/kg
2	800 mg daily	5 mg/kg
3	800 mg daily	7.5 mg/kg
4	800 mg daily	10 mg/kg

562 Poster Session (Board #E1), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM

Efficacy and safety of nivolumab in patients with non-clear cell renal cell carcinoma (RCC): Results from the phase IIIb/IV CheckMate 374 study.

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Background: Initial safety results from the phase 3b/4 CheckMate 374 study showed that flat-dose nivolumab (NIVO) at 240 mg every 2 wk (Q2W) had a consistent safety profile across patients (pts) with clear cell and non-clear cell advanced RCC. We report updated safety and first disclosure of efficacy for pts with non-clear cell RCC (nccRCC) in CheckMate 374. **Methods:** Eligible pts in this cohort were adults with advanced or metastatic nccRCC who received 0–3 prior systemic therapies. Pts received NIVO 240 mg IV Q2W for ≤24 mo or until confirmed progression, unacceptable toxicity, or withdrawal of consent. Pts who benefited after 24 mo continued treatment according to the standard of care. The primary endpoint was incidence of high-grade immune-mediated adverse events (IMAEs). Exploratory endpoints included overall survival (OS), progression-free survival (PFS), objective response rate (ORR), and duration of response (DOR). **Results:** In CheckMate 374, 44 pts had nccRCC. Histological subtypes included papillary (n = 24), chromophobe (n = 7), unclassified (n = 8), and other (n = 5). Most pts with nccRCC (66%) were treatment-naïve. After a median follow-up of 11.1 mo, median OS was 16.3 mo (95% confidence interval [CI] 9.2–not estimable [NE]). OS was similar regardless of baseline PD-L1 expression. ORR was 13.6% (95% CI 5.2–27.4). One pt had complete response (chromophobe histology) and 5 pts had partial response (2 pts with papillary and 1 pt each with chromophobe, collecting duct, and unclassified histology). Median DOR was 10.2 mo (95% CI 5.6–NE). Median PFS was 2.2 mo (95% CI 1.8–5.4). The 1-year PFS rate was 14% (95% CI 5–27). No new safety concerns were identified. No treatment-related grade 5 AEs or grade 3–4 IMAEs were reported. **Conclusions:** Clinically meaningful antitumor activity was observed in the first prospective study of NIVO monotherapy in nccRCC. Responses were observed in several histological subtypes. The safety profile of flat-dose NIVO at 240 IV Q2W is consistent with the initial outcomes reported from this study and across the NIVO program. Clinical trial information: NCT02596035.

563 **Poster Session (Board #E2), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM**

Evolving patterns of metastatic renal cell carcinoma: A meta-analysis.

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Background: Advances in diagnostic and treatment modalities have resulted in better outcomes in metastatic renal cell carcinoma (mRCC) patients. With new therapies extending survival, we hypothesize that pattern of metastatic disease has evolved over time. We assessed the pattern of metastases as reported in baseline characteristics of prospective clinical trial patients between 1990 and 2018. **Methods:** This study identified all phase I-III mRCC therapeutic clinical trials published between January 1990 and July 2018 in PubMed and ClinicalTrials.gov. Studies that included patients with other cancers or did not report metastases were excluded. Data was stratified to examine differences in three listed treatment eras for first-line therapy. Linear regression models were used to evaluate temporal trends and subcategorized as either First Line Only treatments (FLO) or Second-Line and Beyond (SLB). **Results:** 127 clinical trials encompassing 16534 subjects were identified. Between 1990 and 2018, rates of lymph node metastases in the FLO population increased significantly at 1.03% per year ($P < 0.05$). The rate of lung and liver metastases in FLO showed a trend of increase at 0.48% and 0.04% per year, respectively, but decreased -0.73% and -0.15% per year in the SLB population. Moreover, rate of bone metastasis showed a trend of increase in both populations, particularly between the VEGF/TKI and Immunotherapy/TKI eras in the SLB population (18.89% to 29.19%). **Conclusions:** Notable changes were found in the pattern of metastasis in patients with mRCC. Increasing rate of bone metastasis may warrant dedicated bone imaging for routine staging in patients with mRCC. These evolving patterns may have important implications in treatment selection and prognosis in this patient population.

Average % Metastasis.

	Cytokine Era (1990-2004)		VEGF/TKI Era (2005-2016)		Immunotherapy/ TKI Era (2017-2018)		% Change in Metastasis per Year	
	FLO	SLB	FLO	SLB	FLO	SLB	FLO	SLB
% Lung Metastasis	57.81%	17.88%	70.96%	71.03%	68.41%	69.73%	+0.48%	-0.73%
% Liver Metastasis	15.52%	22.52%	20.04%	25.92%	18.29%	17.84%	+0.04%	-0.15%
% Bone Metastasis	22.21%	11.26%	23.22%	18.89%	25.54%	29.19%	+0.20%	+0.60%
% LN Metastasis	37.30%	12.58%	38.22%	32.22%	41.01%	45.41%	+1.03%	+0.60%

564 Poster Session (Board #E3), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM

Treatment-free survival (TFS) after discontinuation of first-line nivolumab (NIVO) plus ipilimumab (IPI) or sunitinib (SUN) in intention-to-treat (ITT) and IMDC favorable-risk patients (pts) with advanced renal cell carcinoma (aRCC) from CheckMate 214.

David F. McDermott, Brian I. Rini, Robert J. Motzer, Nizar M. Tannir, Bernard Escudier, Christian K. Kollmannsberger, Hans J. Hammers, Camillo Porta, Saby George, Frede Donskov, Howard Gurney, Marc-Oliver Grimm, Michael Roger Harrison, Thomas E. Hutson, Shuo Yang, Jennifer Johansen, Sumati Rao, Sabeen Fatima Mekan, Michael Rael, Thomas Powles; Beth Israel Deaconess Medical Center, Boston, MA; Cleveland Clinic Taussig Cancer Institute, Cleveland, OH; Memorial Sloan Kettering Cancer Center, New York, NY; The University of Texas MD Anderson Cancer Center, Houston, TX; U1015 INSERM, Gustave Roussy Cancer Campus, Paris Saclay University, Villejuif, France; University of British Columbia, Vancouver, BC, Canada; UT Southwestern, Dallas, TX; University of Pavia, Pavia, Italy; Roswell Park Comprehensive Cancer Center, Buffalo, NY; Aarhus University Hospital, Aarhus, Denmark; Westmead Hospital and Macquarie University, Westmead, Australia; Jena University Hospital, Jena, Germany; Duke Cancer Institute, Duke University Medical Center, Durham, NC; Baylor Sammons Cancer Center-Texas Oncology, Dallas, TX; Bristol-Myers Squibb, Princeton, NJ; Monter Cancer Ctr, New York, NY; Evidera, San Francisco, CA; Barts Cancer Institute, Royal Free NHS trust, St. Bartholomew's Hospital, London, United Kingdom

Background: TFS characterizes the antitumor activity of immuno-oncology agents after treatment discontinuation. In CheckMate 214, pts with IMDC intermediate/poor-risk aRCC who discontinued first-line NIVO+IPI experienced significantly longer TFS than those who discontinued SUN (McDermott et al, ESMO 2018). Here, we continue the analysis of TFS from CheckMate 214 in ITT and IMDC favorable-risk pts. **Methods:** Pts with previously untreated, predominantly clear cell aRCC were randomized 1:1 to intravenous NIVO 3 mg/kg + IPI 1 mg/kg every 3 weeks for 4 doses followed by NIVO 3 mg/kg every 2 weeks, or oral SUN 50 mg daily for 4 weeks on, 2 weeks off (6-week cycles). TFS was defined as the time from protocol therapy cessation to the start of subsequent systemic anticancer therapy or death, whichever occurred first. TFS in pts who discontinued NIVO+IPI or SUN was compared using Kaplan–Meier methods and log-rank tests. This analysis was conducted for all ITT (NIVO+IPI, 550; SUN, 546) and IMDC favorable-risk (NIVO+IPI, 125; SUN, 124) pts in CheckMate 214. **Results:** Among 463 NIVO+IPI and 477 SUN ITT pts who discontinued protocol therapy, the median TFS was 3.0 months with NIVO+IPI vs 1.3 months with SUN (HR [95% CI]; 0.54 [0.46–0.62]; P<0.0001); the TFS rates 2 years post-discontinuation were 21% vs 7%, respectively. In IMDC favorable-risk pts, 111 and 94 pts discontinued from NIVO+IPI and SUN, respectively. TFS in IMDC favorable-risk pts was also significantly longer with NIVO+IPI vs SUN (median, 6.3 vs 1.1 months; HR [95% CI]; 0.47 [0.34–0.65]; P<0.0001). The TFS rates 2 years post-discontinuation in favorable-risk pts were 29% for NIVO+IPI vs 13% for SUN. **Conclusions:** Similar to the TFS benefit seen in intermediate/poor-risk pts with aRCC, first-line therapy with NIVO+IPI resulted in reduced need for second-line therapy in ITT and IMDC favorable-risk pts compared with SUN. The durable TFS benefit across risk groups despite discontinuation of therapy provides further evidence of the encouraging benefit-risk profile of NIVO+IPI over SUN in pts with previously untreated aRCC. Clinical trial information: NCT02231749.

565 Poster Session (Board #E4), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM

Real-world use of sorafenib for advanced renal cell carcinoma patients with cardiovascular disease: Nationwide survey in Japan.

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Background: The average age of the patients (pts) with renal cell carcinoma (RCC) are getting older year by year, hence the baseline comorbidity should be considered when pts have tyrosine kinase inhibitor treatments. However, the safety and efficacy data of these agents in pts with cardiovascular disease (CVD) are limited. In this study, we analyzed the data which were prospectively collected practical use of sorafenib amongst all RCC pts in Japan, and investigated whether baseline comorbidity of CVD would provide any affection for the safety and efficacy on sorafenib treatment using propensity-matched analysis. **Methods:** A total of 3,255 pts with advanced RCC were enrolled and 770 pts selected by propensity score were matched for CVD (n=385) and non-CVD pts (n=385). Dose modification, tumor response, progression free survival (PFS), and adverse events (AEs) were analyzed. **Results:** After matching the patient's demographics were well balanced except for BMI (22.47 $\pm$ 3.37 vs. 23.13 $\pm$ 3.59, p=0.019) between non-CVD and CVD group, respectively. The median starting dose (800mg vs. 800mg), median daily dose (484.8mg vs. 500mg), and median duration of treatment (7.26 months vs. 7.89 months) were not significantly different. Objective response rate (CR+PR) was comparable in both groups (27.1 and 29.4%). The hazard ratio (HR) of overall PFS was similar between two groups (HR: 1.005, 95% CI: 0.838-1.206). When stratified according to IMDC risk classification, the risk of PFS was not significantly different in any IMDC risk groups (favorable; HR: 0.883, 95% CI: 0.600-1.300, intermediate; HR: 1.11, 95% CI: 0.885-1.3920, and poor ; HR 0.972, 95% CI: 0.513-1.842). Safety was analyzed for 766 pts, and any grade AEs observed $\geq$20% were hand-foot skin reaction (59.5%), hypertension (40.0%), rash (26.9%), lipase/amylase increased (26.5%), and diarrhea (24.2%). The frequency of any grade AEs were similar between the groups, but lipase/ amylase increased was significantly higher in CVD group than that in non-CVD group (p=0.0042). **Conclusions:** The present study suggests that sorafenib can be used with clinical benefit for RCC pts regardless of baseline cardiovascular comorbidities. Clinical trial information: NCT01411423.

566 Poster Session (Board #E5), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM

Impact of body mass index (BMI) on treatment outcomes to immune checkpoint blockade (ICB) in metastatic renal cell carcinoma (mRCC).

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Background: An elevated BMI is associated with improved survival in mRCC patients treated with oral targeted therapies (TT); however, this relationship in the contemporary treatment landscape is unknown. We investigated the effect of BMI on outcomes in mRCC patients treated with PD-1/PD-L1 ICB. **Methods:** We analyzed 147 patients with mRCC who received ICB alone or in combination with VEGF or other therapies. The association of BMI with objective response rate (ORR), progression-free survival (PFS), and overall survival (OS) was evaluated using logistic and Cox regression models, adjusted for known prognostic factors including International Metastatic RCC Database Consortium (IMDC) risk groups, line of therapy, ECOG (0 vs ≥1), and histology. **Results:** Median follow up was 25.5 (4.3-78.6) months (mos). Median time on ICB was 5.1 (< 0.1-69.7) mos. Overall, most patients were male (71%), had clear cell histology (85%), and were intermediate risk (60%). 43% received first-line ICB and 45% received ICB in combination therapy (37% with VEGF inhibition, 8% with other therapies). At ICB initiation, 46 (31%) patients were considered underweight/normal weight (BMI < 25 kg/m^2), 56 (38%) overweight (BMI 25-30 kg/m^2), and 45 (31%) obese (BMI > 30 kg/m^2). Patients with high BMI (≥ 25) had improved OS (median 34.3 vs 16.7 mos, 2-yr OS 61 vs 42%, p = 0.016) compared to those with low BMI (< 25), with an adjusted hazard ratio (HR) = 0.74 (0.44-1.26). ORR (33 vs 28%, p = 0.7) and PFS (median 8.2 vs 5.9 mos, p = 0.4) did not statistically differ. Patients who experienced a BMI change from ≥ 25 at start of first-line TT to < 25 at start of subsequent-line ICB displayed shorter OS (adjusted HR = 2.25 (0.94-5.35)) compared to those with no change. **Conclusions:** High BMI appears to be associated with improved OS in mRCC patients treated with ICB. This contemporary data is consistent with the "obesity paradox" demonstrated in the TT era. Validation with the IMDC database and examination of underlying mechanisms are ongoing.

567 Poster Session (Board #E6), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM

The effect of loss of SETD2 on mitochondrial dysfunction in clear cell renal cell carcinoma.

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Background: SET domain-containing protein 2 (*SETD2*) is among the most commonly mutated genes in clear cell renal cell carcinoma (ccRCC). Classically, *SETD2* modulates chromatin structure via the methylation of lysine 36 on histone H3. However, histone-independent functions of SETD2 are emerging. We sought to discover novel SETD2-dependent changes to the cellular lysine methylation landscape during kidney cancer tumorigenesis. **Methods:** In this study, we used HKC human proximal tubule kidney cell lines, the likely nephrogenic region of origin for ccRCC. The proteomes of wild type (WT) and *SETD2*-knock out (KO) cells were labeled using stable isotope labeling by amino acids in cell culture (SILAC). Proteins were trypsinized and lysine-methylated peptides were immunoprecipitated. Relative abundance of lysine-methylated peptides and total peptides were calculated in the WT and *SETD2*-KO using nano-liquid chromatography/tandem mass spectrometry (LC/MS-MS). **Results:** $>$ 30,000 peptides were quantified, including $>$ 50 lysine methylated peptides. We observed decreased lysine methylation of eukaryotic elongation factor 1A1 (eEF1A1), including K165 trimethylation (K165me3) and K318 monomethylation (K318me1). eEF1A1 is classically known for delivery of aminoacyl-tRNA to the ribosome, and its function is modulated via the lysine methyltranferases eEF1AKMT1-4. eEF1AKMT3 is responsible for trimethylation of K165, and expression of this enzyme was decreased in *SETD2*-KO cells. In addition, we observed significant decrease in expression in proteins of the electron transport chain (ETC) complex 1 in *SETD2*-KO cells yet normal gene expression, suggesting a translational defect. Functionally, *SETD2*-KO cells are characterized by decreased cellular oxygen consumption rate and increased mitochondrial mass, suggestive of ETC dysfunction. **Conclusions:** We observe decreased expression of eEF1AKMT3 in *SETD2*-KO cells, resulting in decreased K165me3 of eEFA1A, decreased translation of ETC proteins, and mitochondrial dysfunction. As mitochondrial dysfunction is commonly observed in RCC, we expect this represents a novel mechanism of *SETD2*-mediated tumorigenesis.

568 Poster Session (Board #E7), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM

Efficacy of targeted therapy (TT) after checkpoint inhibitors (CPI) in metastatic renal cell carcinoma (mRCC): Results from the Canadian Kidney Cancer Information System (CKCis).

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Background: While the use of CPI has demonstrated clinical benefit in patients with mRCC, data showing the efficacy of subsequent TT is limited. This real-world analysis evaluated the efficacy of TT post CPI in mRCC patients. **Methods:** Data was collected and analyzed from CKCis. Patients with mRCC who received TT after CPI were identified and analyzed based on line of therapy. Time to treatment failure (TTF – time from starting first subsequent TT to stopping TT) and overall survival (OS) were calculated. Hazard Ratio (HR) calculations were adjusted for IMDC group and age. **Results:** 102 patients were treated with TT post CPI (table). Those who received first-line ipilimumab + nivolumab (I/N) versus a vascular endothelial growth factor inhibitor (VEGFi) + CPI combination prior to second-line TT had a median TTF of 8.0 vs 5.2 months (m) (HR=0.43, 95% CI: 0.13-1.44) and median OS of 16.5 m vs not reached (HR=0.76, 95% CI: 0.11-5.24). Patients who received a VEGFi versus a mammalian target of rapamycin inhibitor (mTORi) as third-line TT had a median TTF of 7.6 vs 4.4 m (HR=0.52, 95% CI: 0.24-1.10) and median OS of 21.7 vs 16.2 m (HR=0.41, 95% CI: 0.16-1.08). All third-line TT patients received first-line VEGFi and second-line nivolumab. Of the third-line VEGFi TT patients, 24 received axitinib (TTF 7.1 m, OS 21.7 m) and 22 received cabozantinib (data immature). **Conclusions:** Activity of TT in mRCC patients after CPI is demonstrated in multiple lines. In second-line, VEGFi TT had numerically better outcomes after I/N than after VEGFi+CPI combination. Efficacy of third-line TT was seen with a trend favoring VEGFi over mTORi. Axitinib in the third-line has notable activity after CPI, while data on cabozantinib and fourth-line TT are maturing. These results support the use of VEGFi after CPI in mRCC patients.

	Second-line TT	Third-line TT	Fourth-line TT
Total # of pts	27	65	10
Median Age	59	63	70
Male	70%	77%	70%
IMDC group			
Good	15%	18%	30%
Intermediate	69%	54%	40%
Poor	15%	28%	30%
Class of TT			
VEGFi	27	54	8
mTORi	0	11	2
Type of prior CPI			
I/N	10	0	0
VEGFi+CPI	17	0	0
Nivolumab	0	65	10
Median OS (m) (95% CI)	16.5 (10.5-NR)	17.8 (12.4-47.5)	NR
Median TTF (m) (95% CI)	6.2 (3.4-8.9)	7.1 (5.3-8.8)	7.6 (0.5-NR)

NR = Not Reached

569 **Poster Session (Board #E8), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM**

Systematic review and REMARK scoring of renal cell carcinoma (RCC) prognostic circulating biomarker manuscripts.

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Background: No validated biomarkers exist to help guide prognosis of RCC patients. This study seeks to determine the current state of published prognostic RCC biomarker manuscripts and evaluate their quality using the REMARK criteria. **Methods:** The phrase "(renal cell carcinoma OR renal cancer OR kidney cancer OR kidney carcinoma) AND circulating AND (biomarkers OR cell free DNA OR tumor DNA OR methylated cell free DNA OR methylated tumor DNA)" was searched in Embase, Medline and PubMed during March 2018. One author (MI) selected all relevant manuscripts from the search results, and two authors (MI and SP) independently scored all relevant manuscripts using the REMARK guidelines (maximum 20 points comprised of 20 items subdivided into 48 criteria). **Results:** The search identified 525 publications: 73 were valid, 436 were rejected, and 26 were uncertain of their relevance. Amongst the valid publications, 33 were manuscripts of primary research (remainder: 26 review papers, 14 abstracts): manuscripts evaluating $\geq$ 2 biomarkers (n = 8) and novel biomarkers not published elsewhere (n = 7) comprised the majority. The median REMARK score was 10.6 (range 6.4-14.2). All manuscripts stated their marker, study objectives and method of case selection. The lowest scoring criteria were lack of: description of time between storage of blood/serum and marker assay (n = 2); flow or study profile diagram (n = 2); blinding of the person making the marker assessment to clinical outcomes (n = 3); and pre-specified hypotheses (n = 3). In total, only 8 studies reported a hazard or odds ratio. Using Pearson's correlation, there was no association with either year of publication (median 2014; range 2004-2018; r^2 = 0.14; p = 0.44) or impact factor (median 5.168; range 1.2-26.303; r^2 = 0.24; p = 0.17) with REMARK score. **Conclusions:** Despite several published manuscripts on RCC prognostic biomarkers, most poorly adhere to the REMARK guidelines; this may be the cause for the paucity of a validated RCC biomarker to help supplement or supplant current clinical prognostic criteria. Better designed studies and appropriate reporting of methods, results and interpretation are required to address this urgent unmet need.

570 **Poster Session (Board #E9), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM**

Is cytoreductive nephrectomy necessary in metastatic renal cell carcinoma with primary kidney tumor in situ treated by sunitinib: Real-world data from a single Chinese center.

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Background: To evaluate the role of cytoreductive nephrectomy (CN), which was an indispensable treatment in metastasis renal cell carcinoma (mRCC), compared with cytokine treatment, we assessed the survival benefit of CN in patients with mRCC treated by sunitinib in targeted therapy era. **Methods:** This retrospective study compared the progression-free survival (PFS) and overall survival (OS) between mRCC patients who did or did not undergo CN. We screened out and enrolled patients from April 2006 to November 2013 as suitable candidates for CN with primary kidney tumor in situ. Logistic regression models were used to measure the effects of the clinical and pathological covariates. The Kaplan-Meier method and log-rank test were performed to evaluate the possible survival differences between two groups. **Results:** Atotal of 70 patients were assigned to undergo CN followed with sunitinib and 48 received sunitinib alone. According to the survival analysis, the median PFS was 8.38 months and the median OS was 15.48 months, with 109 deaths observed. There were no significant difference between CN-sunitinib group and sunitinib-alone group in both PFS(7.2 versus 11.6 months, 95% confidence interval, 5.3 to 11.8; *P*= 0.525) and OS (16.7 versus 15.2 months, 95% confidence interval, 12.0 to 18.9, *P*= 0.839). However, stratified analysis revealed that PFS and OS might decrease after CN in the subgroups of patients with IMDC prognostic criteria of high-risk disease (PFS: 4.4 [95% CI, 3.5 to 5.3] vs. 6.3 [95% CI, 5.3 to 7.2] months, *P*= 0.002; OS: 8.8 [95% CI, 7.0 to 10.6] vs 9.9 [95% CI, 10.0 to 11.8] months, *P*= 0.011) and those with lymphatic metastasis (PFS: 4.4 [95% CI, 2.9 to 6.0] vs. 6.6 [95% CI, 2.1 to 11.2] months, *P*< 0.001; OS: 8.8 [95% CI, 6.9 to 10.7] vs 9.9 [95% CI, 7.1 to 10.7] months, *P*= 0.006). **Conclusions:** Cytoreductive nephrectomy may offer no survival benefits in those mRCC patients with primary kidney tumor in situ, and moreover, sunitinib-alone therapy perhaps contributes longer PFS and OS for the patients with IMDC high-risk disease and those with lymphatic metastasis.

571 Poster Session (Board #E10), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM

Elevated CD36 expression correlates with increased visceral adipose tissue and predicts poor prognosis in ccRCC patients.

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Background: Growing evidence has proved obesity one of the confirmed important etiologic indicators for renal cell carcinoma (RCC). *CD36* is underpinned to be involved in adipose absorption, but its role in clear cell renal cell carcinoma (ccRCC) remains unclear. This study aimed to investigate the mRNA expression of *CD36* in anthropometric measures of adipose tissue and defining its value in predicting prognosis in ccRCC patients. **Methods:** Real-Time qPCR was detected from 367 paired ccRCC and adjacent normal tissues. Distributions of categorical clinical-pathological data together with levels of *CD36* expression were compared with χ^2-test. Subcutaneous adipose tissue (SAT) and visceral adipose tissue (VAT) were measured by MRI. Pearson's correlation coefficient was utilized to quantify relations between body mass index (BMI), VAT%, SAT and *CD36* expression respectively. Cox regression analysis were developed to address the influence of independent factors on prognostic value. Gene Set Enrichment Analysis (GSEA) was performed to select related genes and pathways from TCGA database. **Results:** In the current study, we demonstrated that *CD36* mRNA was highly expressed in ccRCC tissues, and was found significantly increased in patients with advanced TNM stage (p= 0.003, $p<$ 0.001, $p<$ 0.001), and high VAT% (p= 0.004). Pearson's correlation coefficient indicated *CD36* amplification positively correlated with BMI (r= 0.117, p= 0.025), VAT% (r= 0.465, $p<$ 0.001), while negatively with SAT (r= -0.296, p= 0.002). Furthermore, ccRCC patients with elevated *CD36* expression held shorter PFS and OS, with HR of 4.873 (3.300-7.196, $p<$ 0.001) and 4.610 (2.956-7.189, $p<$ 0.001). In 104 cases whose MRI scans were available, VAT was significantly correlated with poor PFS and OS. Significant genes were obtained from GSEA, and *CD36* was found involved in the most significant pathways including fatty acid metabolism, angiogenesis and TGF-β signaling pathways. **Conclusions:** In conclusion, our study first reveal that elevated *CD36* mRNA expression is positively correlated to distribution of abdominal adipose, particularly VAT%, which, in addition, notably predicts poor prognosis in ccRCC patients.

572 **Poster Session (Board #E11), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM**

Prognostic impact of neutrophil-to-lymphocyte ratio in renal cell carcinoma: A systematic review and meta-analysis.

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Background: Several clinical scores have been adopted in clinical practice for the prognostic estimation in patients with Renal Cell Carcinoma (RCC). Neutrophil-lymphocytes ratio (NLR) has shown to be a reliable and economic parameter associated with prognosis however its role has not been fully understood. **Methods:** We performed a systematic review and meta-analysis according to PRISMA guidelines to evaluate the prognostic value of NLR in terms of overall and progression free survival (OS/PFS) in both metastatic and non metastatic patients with RCC. We applied the inverse variance technique for the meta-analysis of the HRs and due to the intrinsic heterogeneity of the data we adopted a Random Effects model. 24 studies were selected for the final analysis, 21 for the comparison of NLR and OS and 15 for the comparison of NLR and DFS/PFS. **Results:** In overall population higher NLR resulted in worst OS benefit with a pooled HR of 1.80 (95% confidence interval of 1.61 – 2.00, I^2 45%.) as well as in non metastatic (pooled HR of 1.57, 95% CI 1.27-1.94, I^2 39%) and metastatic patients (2.05, 95% CI 1.74-2.41, I^2 0%). Moreover, NLR resulted in worst PFS in overall population (pooled HR 1.69, 95% CI 1.42-2.01, I^2 81%), in non metastatic (HR 1.52, 95% CI 1.23-1.87, I^2 53%) and metastatic (HR 1.95, 95% CI 1.43-2.64 I^2 90%). **Conclusions:** According to our results NLR ratio is a variable correlated to prognosis in RCC patients. The low level of heterogeneity among studies included suggests that it has a strong association with patients' survival. Thus it appears as an attractive, dynamic and economic biomarker which could be adopted to further subdivide prognostic classes into even more accurate groups of prognosis in order to choose the best treatment strategy possible. Further prospective studies are needed to confirm our findings.

573 Poster Session (Board #E12), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM

Real-world clinical outcomes of pazopanib immediately following immunotherapy discontinuation for the treatment of advanced renal cell carcinoma.

Xiting Cao, Derek Tang, Barbara Elizabeth Ratto, Austin Poole, Shoba Ravichandran, Lixian Jin, Wei Gao, Elyse Swallow, Nicholas J. Vogelzang; Novartis Pharmaceutical Corp, East Hanover, NJ; Novartis Pharmaceuticals Corporation, East Hanover, NJ; Novartis, East Hanover, NJ; University of Utah Hunstman Cancer Institute, Salt Lake City, UT; Novartis Oncology, East Hanover, NJ; Analysis Group, Inc., Boston, MA; Comprehensive Cancer Centers of Nevada, Las Vegas, NV

Background: In the first-line setting (1L), pazopanib (PAZ) is recommended by NCCN for treatment of advanced renal cell carcinoma (aRCC). In 2018, immuno-oncology (IO) therapy became commonly used 1L treatment option for aRCC. This study reports real-world clinical outcomes of PAZ following IO therapy among aRCC patients (pts) in an evolving treatment landscape. **Methods:** This retrospective chart review study used medical record data collected by medical oncologists. Included pts were those ≥ 18 at initiation of IO therapy who initiated 2L+ PAZ for clear cell aRCC before November 2017, and had complete medical records from the diagnosis of aRCC to discontinuation of PAZ, death, or the chart extraction date (May 2018), whichever occurred first. Primary outcome was PAZ duration of therapy (DOT). Secondary outcomes were progression-free survival (PFS) and overall survival (OS) since PAZ initiation, reasons for PAZ discontinuation, and adverse events (AEs). Time-to-event outcomes were analyzed by Kaplan-Meier method. **Results:** 258 eligible pts initiated the IO therapies before PAZ as follows: nivolumab (NIVO) (68%), NIVO+ ipilimumab (IPI) (14%), pembrolizumab (12%), and IPI (3%). Ninety-seven (38%), 56 (22%), and 92 (36%) pts were grouped as favorable, intermediate, or poor risk by Heng criteria, respectively. Overall, the median PAZ DOT was 13.4 months (Ms) (95% confidence interval [CI] 10.1-16.0). When stratified by lines of therapy, pts who received PAZ as 2L (n=182) or 3L+ (n=76) had DOT of 13.4 Ms (95% CI 11.1-NR) and 9.6 Ms (95% CI 6.2-NR), respectively. The PFS and OS outcomes are shown in the Table. One hundred-nine (42%) pts reported an AE. The most frequently (>10%) reported AEs were fatigue (29%), diarrhea (14%), decreased appetite (14%), and hypertension (13%). **Conclusions:** In this real-world study, 2+L PAZ following prior IO therapy was well-tolerated, effective, and non-cross-resistant with IO therapy for aRCC pts.

PFS and OS Outcomes.

	Median PFS	Median OS	PFS Rates	OS Rates
	M (95% CI)		12 M	
Overall	13.5 (11.8-NR)	16 (13.5-NR)	0.6	0.9
2L PAZ (N=182)	16.0 (11.8-NR)	16 (16.0-NR)	0.6	0.9
3L+ PAZ (N=76)	13.5 (7.07-NR)	13.5 (13.5-NR)	0.5	0.8

NR=not reached

574 Poster Session (Board #E13), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM

Exploratory endpoints in a FARETES study of the efficacy of testosterone in metastatic renal cell carcinoma (mRCC) patients.

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Background: In multicenter randomized phase 2 study (FARETES) we showed that male patients with mRCC receiving targeted therapy had significantly less fatigue and better symptom control with testosterone undecanoate (T) (MASCC 2018, LBA004). Here we described exploratory endpoints in FARETES study. **Methods:** Sixty male patients with clear cell mRCC, normal PSA level, low testosterone level and no evidence of hypothyroidism receiving first-line sunitinib or pazopanib with fatigue were randomly assigned (1:1) to either T (Nebido, 1,000 mg) and targeted therapy or targeted therapy alone (control group). T was injected intramuscular deeply on Day 1 of a new treatment cycle. Exploratory endpoints included rate of adverse events (AE) of targeted therapy, duration of targeted therapy, objective response rate (ORR), progression-free survival (PFS) and overall survival (OS). **Results:** As of the data cutoff on October 17, 2018, median (range) follow-up was 15.2 (9.9 -16.5) months. No unexpected toxicity of T was observed. Grade 3-4 targeted therapy-related AE occurred in 11 (37%) and 3 (10%) patients in the control group and T group, respectively. Discontinuation due to AE was observed in 3% (1/30) of patients in the T group and in 17% (5/30) of patients in the control group. ORR and PFS were significantly better in the T group (all $P < 0.05$, Table). Median OS was not reached in either group. Clinical trial information: NCT03379012. **Conclusions:** T therapy could decrease rate of serious AE of targeted therapy. Male mRCC patients receiving T had longer duration of targeted therapy, better PFS and ORR. Larger trials are needed to evaluate efficacy of T in this group of patients.

	T group, N = 30	Control group, N = 30
Age (years), mean (range)	52 (33-71)	55 (42-69)
Sunitinib, N (%)	28 (93)	28 (93)
IMDC poor risk factors, 0-2, N(%)	21 (70)	22 (73)
Duration of targeted therapy, median, months (95% CI)	12.8 (10.7-14.2)	8.3 (7-9.6)
ORR, % (N)	50 (15/30)	33.3 (10/30)
PFS, median, months (95% CI)	14.2 (13.4-15.8)	9.6 (8.1-11.5)

575 **Poster Session (Board #E14), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM**

Outcomes of patients with metastatic clear cell renal cell carcinoma treated with second-line VEGFR-TKI after first-line immune checkpoint inhibitors.

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Background: Immune checkpoint inhibitors (ICI) are being increasingly utilized in front-line (1L) setting of metastatic clear-cell renal cell carcinoma (mccRCC). Limited data exist on responses and survival on second-line (2L) VEGFR-TKI therapy after 1L ICI therapy. **Methods:** This is a retrospective study of mccRCC patients treated with 2L VEGFR-TKI after progressive disease (PD) with 1L ICI. Patients were treated at MD Anderson Cancer Center or Memorial Sloan Kettering Cancer Center between December 2015 and February 2018. Objective response was assessed by blinded radiologists' review using RECIST v1.1. Descriptive statistics and Kaplan-Meier method were utilized. **Results:** 70 patients were included in the analysis. Median age at mccRCC diagnosis was 59 years old; 8 patients (11%) had IMDC favorable-risk score, 48 (69%) had intermediate-risk score, and 14 (20%) had poor-risk score. As 1L therapy, 12 patients (17%) received anti-PD-(L)1 monotherapy with nivolumab or atezolizumab, 33 (47%) received nivolumab plus ipilimumab, and 25 (36%) received combination anti-PD-(L)1 plus bevacizumab. 2L TKI therapies included pazopanib, sunitinib, axitinib, and cabozantinib. On 2L TKI therapy, one patient (1.5%) achieved a complete remission (CR), 27 patients (39.7%) a partial response (PR), and 36 patients (52.9%) stable disease (SD), adding to a 94% disease control rate (DCR). Median progression-free survival (mPFS) was 13.2 months (95% CI: 10.1, NA). Estimated 1-yr overall survival (OS) probability was 79.6% (95% CI: 70.2 – 90.3). Median duration of 2L TKI therapy was 10.1 months. In total, 45.7% of subjects required a dose reduction, and 27% of patients discontinued treatment due to toxicity. **Conclusions:** In this retrospective study of patients with mccRCC receiving 2L TKI monotherapy following 1L ICI, we observed 2L antitumor activity and tolerance comparable to historical data for first-line TKI. Further studies are needed to evaluate optimal strategies and sequencing of therapies in mccRCC.

576 Poster Session (Board #E15), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM

Impact of treatment and insurance on socioeconomic disparities on the survival of renal cancer patients in Thailand.

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Background: Access to care is an important aspect of high-quality cancer care. Patients' health insurance status is a factor influencing an individual's ability to access high-quality cancer care. The increased costs of cancer care are negatively impacting patients. 75% of Thai people use the Thailand's Universal Coverage Scheme (UCS), about 15% use the Civil Servant Medical Benefit Scheme (CSMBS) or the Social Security Scheme (SSS). Only CSMBS can reimburse cost of the targeted therapy. Multiple new therapies have emerged for the treatment of metastatic renal cell carcinoma (mRCC) that showed OS increased in following introduction of targeted therapies and immunotherapy. However, many patients lack access to affordable, high-quality cancer care. Aim: To determine the relationship between treatment affordability, insurance status and RCC cancer survival. **Methods:** Retrospectively reviewed 281 medical records of RCC patients at the Ramathibodi hospital between January 2009 and December 2017. We searched the Surveillance, Epidemiology, and End Results dataset. Kaplan–Meier methods and multivariable Cox regression models were used to analyze survival outcomes and risk factors. **Results:** 281 RCC patients, and 127 metastasis were identified. Median age was 59.1 years, and 74.7% were male gender. There were clear cell carcinoma (77.9%), and non-clear cell was 17.1%. IMDC prognostic model categorized as favorable/intermediate/poor risk group as 14.2%/51.2%/29.1%. 41.7% has health insurance status as CSMBS, 7% in SSS and 50.9% in UCS. Only 50% of SSS and UCS paid out of their pocket of mRCC treatment. First line treatment for mRCC were targeted therapy with VEGFR TKI 73.9%, but 26.8% received only supportive care. Median OS was 24 months in the treatment group and only 4.1 months in the best supportive care group ($p < 0.05$). Health insurance status and medication affordability was confirmed as an independent prognostic factor for mRCC patients. **Conclusions:** Insurance status and medication affordability are important predictive factors for mRCC, and improving access to affordable targeted therapies is likely to improve outcomes in mRCC.

577 **Poster Session (Board #E16), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM**

Concordance between PD-L1 assays for metastatic renal cell carcinoma (mRCC) and metastatic urothelial carcinoma (mUC).

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Background: Immune checkpoint inhibitors (ICIs) are now standard of care for mRCC and mUC patients (pts). PD-L1 status is gaining importance as a predictive biomarker, particularly for cisplatin-ineligible mUC. Four different PD-L1 assays vary in thresholds of PD-L1 positivity dependent on tumor type, with limited concordance studies. Given real-world limitations in PD-L1 testing, concordance between assays are needed to distinguish positive (pos)/negative (neg) results and treatment selection. We undertook comparisons of Dako 28-8 and Ventana SP142 assays in mRCC and Dako 22C3 and Ventana SP263 assays in mUC. **Methods:** 32 patients with mRCC and 18 patients with mUC who had received ICI therapy at Duke Cancer Institute were identified. FFPE archival tumor samples for pts with mRCC were evaluated with Dako 28-8 and Ventana SP142 PD-L1 immunohistochemistry (IHC) assays. For pts with mUC, FFPE archival tumor samples were evaluated with Dako 22C3 and Ventana SP263 PD-L1 IHC assays. Scoring was validated by two pathologists using the scoring system for each assay. PD-L1 status was subsequently correlated to best RECIST response (objective response rate (ORR) defined as stable disease or better)). **Results:** The majority of mRCC cases (29/32, 91%) were concordant between Dako 28-8 and Ventana SP142 assays (8 cases pos and 21 cases neg), with 3 discordant cases (1 case pos for Dako 28-8 but neg for Ventana SP142 and 2 cases neg for Dako 28-8 but pos for Ventana SP142). The majority of mUC cases (17/18, 94%) were also concordant between Dako 22C3 and Ventana SP263 assays (2 pos cases and 15 neg cases), with 1 indeterminate Dako 22C3 test due to background lymph node. In mRCC, the ORR for PD-L1 pos cases was 45% (5/11) versus 33% (8/24) for PD-L1 neg cases. In mUC, the ORR for PD-L1 positive cases was 50% (1/2) versus 31% (5/16) for PD-L1 neg cases. **Conclusions:** There was strong concordance between PD-L1 tumor/immune cell assays chosen for comparison in both mRCC and mUC with similar performance characteristics. Although PD-L1 positivity enriches for response to ICIs, many patients respond who are PD-L1 negative. PD-L1 status could be used interchangeably for the majority of cases when selecting treatment in mRCC and mUC.

578 **Poster Session (Board #E17), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM**

A phase II study of cabozantinib as first-line treatment in metastatic collecting ducts carcinoma: The BONSAI trial.

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Background: Metastatic collecting ducts carcinoma (mCDC) is a rare and aggressive disease, characterized by a poor prognosis; its treatment represents an unmet medical need. We aimed to evaluate the activity and safety of cabozantinib (cabo) in mCDC. **Methods:** This is a prospective, monocentric, single-arm phase II trial evaluating cabo in patients (pts) with untreated mCDC. Cabo was administered at the dose of 60 mg orally once daily until disease progression (evaluated by RECIST 1.1 criteria) or unacceptable toxicity. Primary endpoint was objective response rate. Secondary endpoints were progression-free survival, overall survival and safety profile. Exploratory objectives include the identification of somatic mutations and the mutational load on tissue samples; plasma and viable peripheral blood mononuclear cells were studied for immune related biomarker profiling. Results will be crossed with clinical data in terms of response rate, to detect any predictive value of blood immune cell profiling. A central pathological review before study entry is mandatory. The study design is based on a Simon's two stage optimal design: in the first step at least 2 responses in 9 pts enrolled are needed to go to the second stage of the study (14 additional pts). **Results:** From January 2018 to September 2018, 11 pts with mCDC have been so far enrolled, nine of which started study treatment. Median age was 58 years, 8 pts were male and 1 female, 7 pts received a previous nephrectomy. The most common metastatic sites were bone and abdominal lymphnodes (5 pts each), followed by liver and lung (2 pts each). Two pts had a partial response as best response, 2 had a stable disease, 3 had a progressive disease and 3 pts died for early progression. Treatment was feasible and well tolerated. All pts reported at least one grade (G) 1-2 adverse events (AEs): the most common were asthenia, diarrhea, anorexia and nausea, hand-foot syndrome, hypertension and dysgeusia. No G3-4 AEs were reported. Genetic and immunological essays are ongoing to assess the immunomodulatory properties of cabozantinib and potential predictive factors. **Conclusions:** Cabo was safe and active in CDC. The second stage and biomarkers analyses are ongoing. Clinical trial information: NCT03354884.

580 **Poster Session (Board #E19), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM**

Receipt of systemic therapy in older versus younger patients (pts) with metastatic renal cell carcinoma (mRCC).

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Background: More than half of pts diagnosed with mRCC are age 65 or older. However, older pts are often under-accrued/under-represented in clinical trials, partly due to concerns about their ability to tolerate systemic therapy (Rx). Given this, efficacy data from the registration trials may not apply to older pts. Herein, we investigate whether older patients with mRCC are less likely to receive various lines of systemic Rx than their younger counterparts. **Methods:** Clinical data was obtained from a prospectively maintained mRCC registry at the Huntsman Cancer Institute, University of Utah. Older pts were defined as $\geq$65 yrs at initiation of first-line systemic Rx for mRCC. Univariate analyses of the lines of systemic Rx received were performed using the Chi-squared test. Comparison of ordered categorical variables was made with the Wilcoxon rank sum test. **Results:** 264 pts who received first-line Rx for mRCC between 2004-2018 were included, and 108 of them were older pts. For older pts, median age at first-line Rx was 71.1 years and 78.7% had clear cell histology, whereas, the median age for younger pts was 53.4 years and 75.6% had clear cell histology. There was no difference in the baseline IMDC risk categories in older vs. younger pts (p = 0.907). A similar proportion of older and younger pts received at least two lines of systemic Rx (66.9% vs. 62.4%, p = 0.532). Furthermore, when analyzed across all lines of treatment, there was no difference in the number of systemic Rx between older and younger pts (p = 0.593). The median OS was similar in both groups: older 30 months (95% CI 21-44 months) vs. younger 34 months (95% CI 30-46 months) (p = 0.639). **Conclusions:** Older pts with mRCC receive a similar number of systemic Rx as their younger counterparts, and have similar survival outcomes. These findings can inform clinicians when selecting first and salvage-line treatment for older pts, and warrant proportionate accrual and representation of older pts in clinical trials.

581 Poster Session (Board #E20), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM

Outcomes in patients (pts) with advanced renal cell carcinoma (aRCC) who discontinued (DC) first-line nivolumab + ipilimumab (N+I) or sunitinib (S) due to treatment-related adverse events (TRAEs) in CheckMate 214.

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Background: The phase 3 CheckMate 214 trial demonstrated superior efficacy for N+I vs S in aRCC, although more patients discontinued N+I compared with S due to TRAEs. This is a post hoc analysis of outcomes in pts who DC N+I or S due to TRAEs. **Methods:** Untreated pts with clear cell aRCC were randomized 1:1 to N 3 mg/kg + I 1 mg/kg Q3Wx4 (induction) and then N 3 mg/kg Q3W (maintenance), or S 50 mg daily for 4 wk on, 2 wk off (6-wk cycles). This analysis includes all pts who DC due to TRAEs reported during extended follow-up (≤100 d after last study dose). **Results:** Of 550 N+I randomized pts, 135 (25%) DC due to TRAEs, most commonly increased ALT, diarrhea, and increased AST (all 3%); 64 (12%) of 535 S randomized pts DC due to TRAEs, most commonly increased ALT, diarrhea, and pancreatitis (all 1%). In N+I pts who DC due to TRAEs, 47% DC during N+I induction, 7% completed induction but no N maintenance, and 46% completed induction and received N maintenance (median [range] 8 [1–47] doses). At 30-mo minimum follow-up, ORR per investigator, CR rate, and 24-mo OS rate were higher in pts who DC N+I vs S due to TRAEs. Outcomes in pts who DC S due to TRAEs were similar to those in all S ITT pts and worse than in N+I pts who DC due to TRAEs (Table). At 24 mo, 42% of pts who DC N+I due to TRAEs were alive and free from second-line therapy. Consistent outcomes were seen in pts who DC N+I due to TRAEs across IMDC risk groups (data to be presented). Pts who DC N+I due to TRAEs experienced more immune-related select TRAEs and received more high-dose steroids (≥40 mg prednisone daily or equiv.), but times to onset and resolution and resolution rates of select TRAEs were similar vs all treated N+I pts. **Conclusions:** Discontinuation of first-line N+I due to TRAEs did not result in impaired outcomes, and a high proportion of pts remain alive and free from second-line therapy. Clinical trial information: NCT02231749.

	All		Who DC	
Arm; n	**N+I; 550**	**S; 546**	**N+I; 135**	**S; 64**
ORR	41	34	47	33
(95% CI), %	(37–46)	(30–38)	(38–55)	(22–46)
CR, %	11	2	12	3
PR, %	31	32	35	30
SD, %	30	41	29	48
PD, %	22	16	16	0
mOS	NR	37.9	NR	NR
(95% CI), mo	(NE–NE)	(32.2–NE)	(NE–NE)	(18.2–NE)
HR (95% CI)	0.71 (0.59–0.86)		0.70 (0.42–1.15)	
OS at 24 mo, %	71	61	74	61

NE, not estimable; NR, not reached

582 **Poster Session (Board #E21), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM**

Are immune checkpoint inhibitors (ICI) a valid option for papillary renal cell carcinoma (pRCC)? A multicenter retrospective study.

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Background: pRCC is the most common non-clear cell RCC (nccRCC) and represents up to 15% of RCC. Pivotal studies evaluating ICI mostly excluded nccRCC. Therefore the efficacy of ICI in pRCC remains to be demonstrated. **Methods:** We retrospectively investigated the activity and safety of PD-1/PD-L1 inhibitors (PD-1i) specifically in patients (pts) with metastatic pRCC from 15 centers in France and Belgium. Pts baseline characteristics, treatment outcome and safety were collected. Primary endpoint was time-to-treatment failure (TTF). Secondary endpoints included objective response rate (ORR), overall survival (OS) and treatment-related adverse events (TRAEs). **Results:** From 02/2016 to 09/2018, 50 pRCC pts treated with PD-1i were included. Median age was 63 years (range: 27-84), 36 (72%) were male. Histology included 14 (28%) type 1 pRCC, 30 (60%) type 2 pRCC, 6 (12%) unclassified pRCC. PD-1i was used in first line setting in 5 pts (10%), in second line in 29 pts (58%) and in third line or beyond in 16 pts (32%). IMDC risk group at PD-1i start was 22% good, 44% intermediate and 33% poor. ICI used were PD-1 inhibitors in 47 pts (94%) and PD-L1 inhibitors in 3 pts (6%). PD-1 in was used as monotherapy in 94% of pts. With a median follow up of 10.7 months (95% Confidence Interval (CI): 6.8-14.8), the median TTF was 3.7 months (95% CI: 3.1, 10.1). In type 1, the median TTF was 7.1 months (95% CI: 3.2-NA) and 3.2 months (95% CI: 2.9-NA) in type 2. Median treatment duration was 3.2 months (range: 0.4-24.5, IQR: 2.4-6.4). Among the 45 pts evaluable for ORR, best response was complete response/partial response in 8 pts (16%), stable disease in 13 pts (26%) and progressive disease in 24 pts (48%). ORR was 25% in type 1 pRCC and 15% in type 2 pRCC. Median OS was 17.6 months (95% CI 11.4- not reached). TRAEs of grade 3-4 were noted in 6 patients (12%) which led to treatment discontinuation, no grade 5 were observed. **Conclusions:** This retrospective study is the largest cohort of metastatic pRCC treated with PD-1i to date. PD-1i exhibit limited activity in this pRCC population, with better TTF and ORR in type 1 pRCC. Our findings underline the need for further prospective clinical trials evaluating ICI combinations in pts with pRCC.

583 Poster Session (Board #E22), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM

RNAseq in addition to next generation sequencing in advanced genitourinary cancers reveals transcriptomic silencing of DNA mutations: Implications for resistance to targeted therapeutics.

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Background: Next generation sequencing (NGS) for advanced tumors is becoming more routine. However, not all patients respond to precision matched treatments. We hypothesized that one potential reason for treatment failure with targeted therapy could be discrepancies between DNA alterations and RNA expression. **Methods:** Tumor samples from patients with metastatic kidney, bladder, and prostate cancer were analyzed by whole exome or whole genome NGS and RNA sequencing (CLIA-certified laboratory; NantOmics LLC, Santa Cruz, CA). Only known pathogenic driver alterations were analyzed in the current study. **Results:** Of 45 patients, 10 had kidney cancer, 18 had bladder cancer; and 17 had prostate cancer. Median age was 66 years (range, 28 - 86). The most commonly altered genes were *TP53* (35.6% [16/45]), *PIK3CA* (15.6% [7/45]), *FGFR3* (11.1% [5/45]), *ALK* (8.9% [4/45]), and *ATM* (8.9% [4/45]). In total, 86 pathogenic DNA alterations were identified; 17 of these (19.8%) were not observed at the RNA level. Among 45 patients, 31.1% (14/45) had ≥1 DNA alteration that was not expressed at the RNA level. Discordance between DNA and RNA was seen in 40% of patients with kidney cancer (4/10), 28% of patients with bladder cancer (5/18), and 29% with prostate cancer (5/17). Examples of genes that had pathogenic DNA alterations not seen at the RNA level included *ALK* (four discordant cases), *KDR* (three discordant cases) and *GNAS* (one discordant case). On the other hand, alterations involving certain genes showed 100% concordance between DNA and RNA: *TP53* [N = 16], *PIK3CA* [N = 7], and *FGFR3* [N = 5]). **Conclusions:** A significant number of patients with genitourinary tumors had DNA alterations that are silenced at the RNA level (19.8%). Transcriptomic silencing merits additional investigation as a mechanism that could mediate resistance to therapeutics targeted at cognate alterations.

584 **Poster Session (Board #F1), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM**

First-line (1L) immuno-oncology (IO) combination therapies in metastatic renal cell carcinoma (mRCC): Preliminary results from the International Metastatic Renal Cell Carcinoma Database Consortium (IMDC).

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Background: In mRCC, ipilimumab and nivolumab (ipi-nivo) is a 1L treatment option. Recent data have also shown efficacy of 1L PD(L)1-VEGF (PV) inhibitor combinations. The efficacy of these two strategies has not been compared. **Methods:** Using the IMDC dataset, patients (pts) treated with any 1L PV combination were compared to those treated with ipi-nivo. Multivariable Cox regression analysis was performed to control for imbalances in IMDC risk factors. **Results:** 164 pts received 1L IO combination therapy: 104 treated with PV combinations and 60 with ipi-nivo. Baseline characteristics and IMDC risk factors were comparable between groups (Table). When comparing PV combinations vs ipi-nivo, 1L response rates (RR) were 30% vs 39% (p = 0.29), time to treatment failure (TTF) was 13.2 (95% CI 8.3-16.1) vs 8.5 months (95% CI 5.7-14.0, p = 0.31), and median overall survival (OS) was not reached (NR) (95% CI 19.7-NR) vs NR (95% CI 27.6-NR, p = 0.39). When adjusted for IMDC risk factors, the hazard ratio (HR) for TTF was 0.77 (95% CI 0.44-1.35, p = 0.36) and the HR for death was 0.94 (95% CI 0.33-2.71, p = 0.91). Similar results were seen when restricting the cohort to IMDC intermediate/poor risk pts only. In pts receiving subsequent VEGF TKI monotherapy, second-line (2L) RR (13% vs 45%, p = 0.07) and TTF (5.5 vs 5.4 months, p = 0.80) for PV combinations (n = 15) vs ipi-nivo (n = 20) were not significantly different. **Conclusions:** There does not appear to be a superior 1L IO combination strategy in mRCC, as PV combinations and ipi-nivo have comparable RR, TTF and OS. Although there is a trend towards differences in RR, there does not appear to be a significant difference in TTF for patients receiving 2L VEGF TKI therapy.

	PD(L)1-VEGF (N = 104)	Ipi-Nivo (N = 60)
IMDC Risk Groups		
Favourable	25/61 (41%)	10/42 (24%)
Intermediate	27/61 (44%)	25/42 (60%)
Poor	9/61 (15%)	7/42 (17%)
IMDC Risk Factors		
KPS < 80	2/89 (2%)	2/57 (4%)
Diagnosis to therapy < 1 yr	58/104 (56%)	30/60 (50%)
Calcium > ULN	7/77 (9%)	8/48 (17%)
Hemoglobin < ULN	35/94 (37%)	25/55 (46%)
Neutrophils > ULN	11/87 (13%)	7/49 (14%)
Platelets > ULN	11/93 (12%)	9/54 (17%)

*All non-significant ($p > 0.05$)

585 Poster Session (Board #F2), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM

Sites of metastasis (mets) and association with clinical outcomes (CO) in metastatic renal cell carcinoma (mRCC) patients (pts) treated with cabozantinib (cabo).

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Background: Cabo is approved for the treatment for mRCC. We investigated the association of sites of mets and clinical outcomes (CO) in mRCC pts treated with cabo. **Methods:** We performed a retrospective analysis of 65 mRCC pts treated with cabo at Winship Cancer Institute from 2016 to 2018. Overall survival (OS) and progression-free survival (PFS) were measured from first dose of cabo to date of death and clinical or radiographic progression, respectively. Objective response was defined as a complete response (CR) or partial response (PR). Sites of mets were obtained from radiology and clinic notes and included bone, lymph node, brain, lung, and liver. Univariate analysis (UVA) and multivariate analysis (MVA) was performed using Cox proportional hazard or logistic regression model. **Results:** The median age was 63 years and most (68%) were males. The majority of pts (79%) had ccRCC and 48% received at least 2 prior systemic treatments. The distribution of mets were: bone (42%), lymph node (69%), brain (6%), lung (83%), and liver (40%). The UVA and MVA of association between sites of mets and CO are presented in Table. Pts with bone mets had significantly longer OS in UVA and trended towards longer OS and PFS in MVA compared to pts without bone mets. **Conclusions:** Bone mets may be a prognostic factor for improved CO in mRCC pts treated with cabo. Larger studies are needed to validate the results of this study. UVA and MVA† of bone metastases and CO.

	OS		PFS		OR*	
	HR (CI)	p-value	HR (CI)	p-value	OR** (CI)	p-value
UVA	2.62 (1.14-5.99)	0.023***	1.63 (0.89-2.99)	0.111	0.65 (0.20-2.12)	0.470
No vs. Yes Bone mets						
MVA	2.63 (0.90-7.71)	0.078	1.35 (0.66-2.72)	0.409	1.37 (0.29-6.55)	0.691
No vs. Yes Bone mets						
No - Bone Mets (n=38)	**Median OS:** 7.5 months		**Median PFS:** 3.7 months		**Response Rate:** 16%	
Yes - Bone Mets (n=25)	**Median OS:** 19.9 months		**Median PFS:** 6.2 months		**Response Rate:** 22%	

†Multivariable model controlled for gender, race, IMDC risk group, number of distant metastases, age, and ccRCC *Objective response: probability of PR+CR were modeled. **Odds ratio ***statistical significance at alpha < 0.05.

586 Poster Session (Board #F3), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM

Angiogenic factor and cytokine analysis among patients with renal cell carcinoma treated with adjuvant VEGFR TKIs.

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Background: VEGFR TKIs are important therapeutic agents in RCC, but their adjuvant use remains limited. Investigating the effects of these medications on circulating angiogenic factors and cytokines in the adjuvant setting can elucidate whether changes in cytokine levels result from drug-host or drug-tumor interactions, and may reveal biomarkers to guide patient selection for adjuvant treatment. **Methods:** In the ECOG-ACRIN 2805 (ASSURE) trial, patients with resected RCC were randomized to sunitinib, sorafenib, or placebo. Plasma was collected at start of treatment and 4 or 6 weeks after treatment initiation. All paired samples available by July 2010 were analyzed, corresponding to 413 patients. We analyzed VEGF, PlGF, sFlt1, KDR/sVEGFR-2, Ang2, bFGF, HGF, IFNg, IL8, CXCL9, CXCL10, and CXCL11. Mixed effects models were used to test for changes from baseline. Cox models were used to assess associations between disease-free survival (DFS) and angiogenic factor and cytokine levels. **Results:** VEGF and PlGF increased after 4 weeks on either treatment ($p < 0.0001$ for both), and at 6 weeks VEGF and PlGF levels returned to baseline for patients on sunitinib (corresponding to the 2 week break in the sunitinib schedule) but not sorafenib. Levels of sFLT-1 decreased after 4 weeks on suntinib and after 6 weeks on sorafenib ($p < 0.0001$). sVEGFR2 decreased after both 4 and 6 weeks of treatment on both sunitinib and sorafenib ($p < 0.0001$). Patients on placebo had no significant changes in circulating angiogenic factor or cytokine levels. CXCL-10 levels increased after 4 weeks on both sunitinib and sorafenib but not on placebo, and remained elevated at 6 weeks on sunitinib. Higher baseline CXCL-10 was associated with worse DFS (HR 1.41 per log increase in CXCL-10, Holm adjusted p-value 0.003, 95% CI 1.18-1.70). This remained significant after adjustment for T-stage, Fuhrman grade, and ECOG PS. **Conclusions:** Among patients treated with VEGFR TKIs in the adjuvant setting for RCC, drug-host interactions mediate changes in cytokines and angiogenic factors. Elevated CXCL-10 prior to treatment was associated with higher recurrence risk. Studies to understand the functional consequences of these changes are underway.

587 Poster Session (Board #F4), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM

Neoadjuvant durvalumab +/- tremelimumab affects the expression of immune checkpoint (IC) molecules on myeloid derived suppressor cells (MDSC) in patients (pts) with locally advanced renal cell carcinoma (RCC).

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Background: In a single arm, open label phase 1b clinical trial the safety of neoadjuvant durvalumab +/- tremelimumab was studied in pts with (w) locally advanced RCC. Expression of IC molecules on immunomodulatory cells in peripheral blood (PB) and tumor (T) and the association w treatment (tx) was investigated. **Methods:** Pts with ≥ T2bN0-1M0 RCC received either durvalumab or combination durvalumab + tremelimumab prior to surgery. Blood samples were drawn prior to neoadjuvant tx, prior to surgery, and approximately 30 days after surgery before adjuvant tx. The percentage of MDSC (CD33+/HLADR-) and subtypes in PB and T and expression of PD1, PD-L1, and V-domain Ig suppressor of T cell activation (VISTA) were measured. MDSC subtypes included polymorphonuclear (PMN; CD15+/CD14-), monocytic (M; CD15-/CD14+) and uncommitted (UC; CD15-/CD14-). Linear mixed model was used for each MDSC subtype to estimate and compare cohorts over time. **Results:** Eighteen pts were enrolled: 4 women and 14 men, median age 62, 17 pts had T3-4 and 4 pts had N1 disease. Six pts received 1 dose of durvalumab and 12 pts received 1 dose of durvalumab + tremelimumab before surgery. Tx-related grade 3 adverse events (per CTCAE, v5.0) included thrombocytopenia, bilateral lower extremity weakness, hyperglycemia, chest pain, and diabetic ketoacidosis.One pt had grade 4 elevated lipase. One pt had sudden death from a non-drug related cardiac event 9 days after receiving combination therapy prior to surgery. PB and T samples from 17 pts were available. Expression of VISTA on M-MDSC and UC-MDSC were positively correlated in PB and T (Spearman's rho = 0.61; P=0.03 for both). VISTA expression on UC-MDSC in PB was significantly higher in pts who received durvalumab monotherapy compared to those treated w durvalumab + tremelimumab (P=0.04). Frequencies of PD-L1 expression on M-MDSC and UC-MDSC in PB decreased significantly from pre- to post-neoadjuvant tx ($P < 0.01$). **Conclusions:** Neoadjuvant durvalumab + tremelimumab in pts w locally advanced RCC is feasible and affects the expression of IC molecules (PD-L1 and VISTA) on M-MDSC and UC-MDSC. Clinical trial information: NCT02762006.

588 **Poster Session (Board #F5), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM**

Eficacy and safety of first-line TKI in elderly with metastatic renal cancer.

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Background: Data on 1st line treatment with tyrosine kinase inhibitors (TKI) in elderly patients(pts) with metastatic renal cell carcinoma (mRCC) is controversial, and there is rationale for inferior outcomes due to multiple comorbidities and polypharmacy. We aimed to compare the efficacy and safety between the elderly (E) and non-elderly (NE) in 1st line therapy, and to explore factors influencing survival and toxicity. **Methods:** We retrospectively reviewed all medical records of mRCC pts treated with 1st line TKI at our institution (2007 – 2018). Categorial variables were compared by Fisher's exact test and continuous, Mann–Whitney. Survival was estimated by Kaplan-Maier method, prognostic factors adjusted by Cox regression model. **Results:** From 171 eligible pts, 64 (37.4%) had ≥ 65years old, with median age of 70.5 for E and 56 for NE. In both groups most were male, had clear cell histology, good/intermediate IMDC risk, prior nephrectomy and > 1 metastatic (mets) site. Sites of mets were evenly distributed. E pts had more diabetes (35.9 vs16.8%, p.009) , hypertension (67.2 vs 46.7%, p.01), cardiovascular disease (15.6 vs 6.5%, p.06), moderate/severe renal dysfunction (62.5 vs 28.8%, p < 0001), high Charlson Comorbidities Index (CCI≥3, 48.4% vs 20.8%, p < .0001), polypharmacy (34.4 vs15.9%, p.008), worst ECOG (≥2, 28.2 vs 12.3%, p.01), and a trend to worst nutrition (weight loss 35.9 vs 22.5%, p.07). Sunitinib was used for 60.9 vs 79.4%, Pazopanib 35.9 vs 18.7%, Sorafenib 3.1 vs 1.9%, comparing E and NE pts. Median overall survival (OS) and progression free survival (PFS) was 23.7 vs 25.6m (p.8) and 9.3 vs 10.9m (p.7), respectively. After adjusting for prognostic factors, age continues not to influence OS (HR 1.17, IC95 0.77-1.78, p.45). Grade (G) 3/4 toxicity was seen in 59.4 vs 53.3%, dose reduction in 54.7 vs 53.3% and suspension due to toxicity 25 vs 13.3% for E and NE, respectively. In the E, none of the comorbidities, CCI or polypharmacy impaired OS or toxicity, but pts using sunitinibe had greater G3/4 toxicity than with pazopanib (71.8 vs 39.1%, p.02). **Conclusions:** Elderly had similar outcomes to NE pts, despite greater comorbidities and polypharmacy, hence efficacious therapies shouldn't avoided. Pazopanib seems to be safer in this subgroup.

589 Poster Session (Board #F6), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM

Characterization of tumor mutational burden (TMB), PD-L1, and DNA repair genes to assess correlation with immune checkpoint inhibitors (ICIs) response in metastatic renal cell carcinoma (mRCC).

Matthew Labriola, Jason Zhu, Rajan Gupta, Shannon McCall, Jennifer Jackson, James R White, Elizabeth Weingartner, Eric Kong, Peter Simone, Eniko Papp, Kelly Gerding, John Simmons, Daniel J. George, Tian Zhang; Duke Medical Center, Durham, NC; Duke Cancer Institute, Duke University, Durham, NC; Duke University Medical Center, Durham, NC; Personal Genome Diagnostics, Inc., Baltimore, MD; Duke Cancer Institute, Durham, NC

Background: ICIs have revolutionized treatment for mRCC; however there are limited predictive biomarkers for response to ICIs. PD-L1 status is still controversial demonstrating little predictive utility in mRCC. TMB is predictive for response to ICIs in melanoma and non-small cell lung cancer (NSCLC), but has not been validated in mRCC. Here, we assess the correlations between TMB and PD-L1 status with outcomes to ICI treatment in mRCC. **Methods:** 34 patients (pts) with mRCC who had previously received ICI therapy at Duke Cancer Institute were identified. Tumor samples were retrospectively evaluated using a Personal Genome Diagnostics Assay for somatic variants across $>$ 500 genes, as well as TMB and microsatellite status. Tumor samples were also analyzed with the Dako 28-8 PD-L1 IHC assay. Deidentified clinical information was extracted from the medical record and tumor response was evaluated based on RECIST criteria. **Results:** Pts were grouped by overall response following ICI therapy into either progressive disease ("PD", n = 18) or disease control group ("DC", n = 16), defined as either stable disease, partial response, or complete response. Pts displayed a TMB range from 0.36 to 12.24 mutations/Mb with a mean score of 2.83 muts/Mb, with no significant difference between the PD and DC groups (mean 3.01 muts/Mb vs. 2.63 muts/Mb, $p > 0.05$). 9 of 32 evaluable samples were PD-L1 positive, with 4 in the PD group and 5 in the DC group. Notably, the DC group displayed a significant enrichment of mutations in genes affiliated with DNA repair (including BRCA1, BRCA2, FANCA, FANCB, FANCG, FANCM, MSH3, MSH6, RAD50, RAD51C, RAD51D, RAD54B, RECQL4, and SLX4; $p = 0.0444$). **Conclusions:** Overall, in this mRCC cohort, neither TMB nor PD-L1 correlated with patient outcomes or with ICI response. Furthermore, high TMB was not significantly associated with PD-L1 expression within the samples. The higher frequency of mutations in DNA repair genes in the DC group suggests potential use as a predictive signature for ICI response, warranting future prospective studies.

590 Poster Session (Board #F7), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM

Efficacy of alpha-1,3-galactosyltransferase-expressing allogeneic renal cell carcinoma immunotherapy in patients (pts) with refractory metastatic renal cell carcinoma (mRCC).

Andrew W Hahn, Charles G. Drake, Samuel R. Denmeade, Yousef Zakharia, Benjamin Louis Maughan, Eugene Paul Kennedy, Charles J. Link, Nicholas N. Vahanian, Hans J. Hammers, Neeraj Agarwal; University of Utah Hunstman Cancer Institute, Salt Lake City, UT; Columbia University Herbert Irving Comprehensive Cancer Center, New York, NY; Johns Hopkins University Sidney Kimmel Comprehensive Cancer Center, Baltimore, MD; Georgia Regents University, Augusta, GA; Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins University, Baltimore, MD; Thomas Jefferson University, Phoenixville, PA; NewLink Genetics Corporation, Ames, IA; UT Southwestern, Dallas, TX; Huntsman Cancer Institute, University of Utah, Salt Lake City, UT

Background: HyperAcute Renal (HAR) immunotherapy consists of two allogeneic renal cancer cell lines that have been genetically modified to express α(1,3)Gal, to which humans have an inherent pre-existing immunity. A previous report demonstrated that HAR is well tolerated in pts with mRCC (2017 GUASCO, abstract: 528). Herein, we report the efficacy of HAR immunotherapy in mRCC. **Methods:** Pts with refractory clear-cell mRCC were eligible for this phase 1 dose-escalation trial. Concomitant treatment (Rx) with other approved agents was permitted after initial 2 months (m) of HAR monotherapy. The trial followed a standard 3+3 design with cells injected intradermally weekly for 4 weeks then biweekly injections for 10 immunizations (150 x10^6cells then escalated to 300 x10^6cells). Co-primary objectives were safety and efficacy. **Results:** A total of 18 patients were enrolled (4 low dose, 14 high dose) between 06/2015 to 07/2016. Patients received a median of 1 systemic Rx prior to HAR immunotherapy, with 8 patients receiving 2 or more prior agents. IMDC risk categories at the time of initial metastatic disease were: favorable risk (33%), intermediate risk (66%), poor risk (0%). The ORR was 0% with a disease control rate of 50%. Median PFS for patients treated with HAR immunotherapy was 2.0 months (m) (range 1.7-30.3 m). For patients receiving the low dose HAR, median overall survival (OS) was 14.2 m (range 3.6-21.6 m), while median OS for high dose HAR was 25.3 m (5.8-29.3 m). At the time of data cutoff in 09/2018, 7 patients were still living. Detailed clinical data will be presented in the meeting. **Conclusions:** HAR immunotherapy in refractory mRCC was well tolerated and demonstrated potential efficacy for OS similar to currently approved salvage-line Rx. With a unique mechanism of action, HAR immunotherapy may be a candidate for inclusion in novel combinatorial regimens being developed in salvage therapy setting in pts with mRCC. Clinical trial information: NCT02035358.

591 **Poster Session (Board #F8), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM**

Expectations of cure among patients with advanced genitourinary cancer treated with immunotherapy.

Cristiane Decat Bergerot, Paulo Gustavo Bergerot, Errol James Philip, Joann Hsu, Nazli Dizman, Ulka N. Vaishampayan, Tanya B. Dorff, Sumanta K. Pal; City of Hope Comprehensive Cancer Center, Duarte, CA; City of Hope Comprehensive Cancer Center, Monrovia, CA; University of California San Francisco, San Francisco, CA; City of Hope, Duarte, CA; Karmanos Cancer Institute, Detroit, MI

Background: Over the past 15 years, considerable progress has been made in systemic therapy options for genitourinary (GU) cancers. In diseases such as metastatic renal cell carcinoma (RCC) and urothelial cancer (UC), immunotherapeutic strategies such as programmed death-1 (PD-1) or programmed death-ligand 1 (PD-L1) inhibition have elicited durable responses, albeit in a minority of patients. We examined expectations for clinical outcome with immunotherapy among patients with advanced GU cancers. **Methods:** A survey study was conducted in patients with advanced GU cancers initiating PD-1/PD-L1 inhibitors from October 2017 to September 2018. Patients were screened prior to initiation of immunotherapy for their expectation of cure (divided into 4 quartiles), symptoms of anxiety and depression (PROMIS-A and PROMIS-D), and quality of life (QOL; FACT-G). For purposes of the survey, cure was equated to a durable complete response. Differences in frequency of anxiety, depression and QOL were compared amongst subsets of patients divided by expectation of cure. **Results:** Among 60 patients, median age was 67, 72% were male and 81% were married. Types of cancer included RCC (69%), UC (19%) and prostate cancer (12%). The majority were in the 1st or 2nd line of therapy (40% and 31%, respectively). Despite extensive counseling from GU medical oncologists, 23% of patients thought that cure was "very likely", defined as in the range of 76-100%. Approximately 70% of patients estimated cure in the range of 0-25%, in line with clinical counseling. These patients had higher rates of anxiety (P = 0.01), depression (P = 0.002) and poorer QOL (P = 0.003) compared to patients who felt cure was very likely. **Conclusions:** A considerable proportion of patients with advanced GU malignancies harbor unrealistic expectations around the potential benefit of immunotherapy. Although a first instinct may be to remedy these expectations, it is important to bear in mind that these patients had better emotional well-being and QOL. We will validate these findings and assess these parameters longitudinally in an upcoming SWOG trial for patients with mRCC receiving upfront immunotherapy.

592 Poster Session (Board #F9), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM

The significance of insulin receptor expression to predict the resistance to VEGFR-TKIs and induce PD-L1 expression in advanced clear cell renal cell carcinoma.

Masayuki Takahashi, Kei Daizumoto, Tomoya Fukawa, Yayoi Fukuhara, Keisuke Ozaki, Megumi Tsuda, Yoshito Kusuhara, Hidehisa Mori, Yasuyo Yamamoto, Kunihisa Yamaguchi, Tomoharu Fukumori, Hiroomi Kanayama; Department of Urology, Tokushima University Graduate School of Biomedical Sciences, Tokushima, Japan

Background: Previously we have identified the prognostic gene set of ccRCC patients, where insulin receptor (INSR) expression was decreased in the patients with poor outcome (Proc Natl Acad Sci U S A., 2001). We examined the clinical significance of decreased INSR expression and sought to elucidate the underlying mechanisms. **Methods:** The INSR expression was immunohistochemically examined in the nephrectomy specimens of RCC patients (n = 33) who then received axitinib. We established patient derived Xenograft model (PDX) of ccRCC and examined the INSR expression in the axitinib resistant PDX tumors by Western blotting. As the INSR is expressed in the vascular endothelial cells, we co-cultured the RCC cell lines with the human renal glomerular endothelial cells (HGEC) treated with si-RNA of INSR (si-INSR) and the microarray experiment was conducted. **Results:** In RCC patients with axitinib, those with low INSR expression had poor outcome (median PFS 19.5 vs 2.3 months, $p < 0.001$; median OS 34.2 vs 5.6 months, $p = 0.001$). The INSR expression was the significantly independent predictor of PFS ($p = 0.006$). In the axitinib-resistant PDX tumors, the expression of INSR was decreased. In the co-culture experiments, the microarray experiments revealed that the decreased INSR expression in the HGECs may be involved with the important signaling pathway including interferon response in Caki-1 cells. Interferon- β was highly expressed in HGECs with si-INSR. The decreased INSR expression and the increased interferon-β expression in HGEC were confirmed when axitinib was administered. The Caki-1 cells that was co-cultured with HGECs treated with si-INSR demonstrated high expression of PD-L1. The PD-L1 expression was increased in a concentration-dependent manner of recombinant interferon-β and increased phosphorylation of STAT1 and STAT3 were observed. **Conclusions:** In conclusion, the decreased INSR expression could be a biomarker to predict the resistance to VEGFR-TKIs. The decreased INSR expression was correlated with the increased interferon-β expression in HGECs, which leads to the induction of PD-L1 through increased phosphorylation of STAT1 and STAT3.

593 Poster Session (Board #F10), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM

Synchronous and metachronous cases of renal cell carcinoma and hematologic malignancies in a state cancer registry.

John Clark Henegan, Katelyn Mitchell, Joseph Maher; University of Mississippi Medical Center, Jackson, MS

Background: A Swedish national family-cancer database reported an association between renal cell carcinoma (RCC) and hematologic malignancies within families. Our hypothesis was that a search of a state cancer registry would detect an increased incidence of observed (versus expected) synchronous and metachronous cases of RCC and select hematologic malignancies. **Methods:** A query of the Mississippi Cancer Registry was performed for synchronous ($<$ 6 months between diagnoses) and metachronous ($>$ 6 months) cases of RCC and select hematologic malignancies (non-Hodgkin lymphoma (NHL), multiple myeloma (MM), chronic lymphocytic leukemia (CLL), chronic myeloid leukemia, and Hodgkin lymphoma) in the state from 2003 to 2013. The expected number of cases was calculated based on crude case numbers available from https://www.cancer-rates.info/ms/. The percentage of the population $<$18 years of age was removed from the eligible population. 2x2 tables were constructed to calculate a chi-square score of expected versus observed cases. Using one degree of freedom, a p-value was calculated from this statistic. Due to privacy issues, the registry was unable to provide an exact number of observed combined cases if there were $<$ 5 in the time period. **Results: Conclusions:** There is a statistically significantly increased incidence of observed (versus expected) synchronous and metachronous cases of RCC with the B-cell malignancies NHL, MM, and CLL in Mississippi between 2003 and 2013. Future research will focus on clinical characteristics of patients with synchronous or metachronous cases of RCC and these hematologic malignancies.

Malignancy	Individual Cases, 2003-2013	Expected Combined Cases, 2003-2013	Observed Combined Cases, 2003-2013 (Synchronous, Metachronous)	Chi-Square Statistic, p-value
Renal Cell Carcinoma	6191	Not applicable	Not applicable	Not applicable
Non-Hodgkin Lymphoma	5862	17	27 (8,19)	0.008
Multiple Myeloma	2445	7	21 (8, 13)	$<$ 0.00001
Chronic Lymphocytic Leukemia	1247	4	18 (at least 2*, 16)	$<$ 0.00001
Hodgkin Disease	805	3	Too Few to Report	--
Chronic Myeloid Leukemia	513	0	Too Few to Report	--

***: Registry indicated between 2-5 cases occurred – unable to give exact number due to privacy concerns**

594 Poster Session (Board #F11), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM

Investigation of IMPDH2 overexpression in renal cell carcinoma (RCC) & its association with oncologic outcomes.

Arun Sendilnathan, Ramya Krishna Velagapudi, Alejandro Marinos Velarde, Roman Jandarov, Zheng Zhu, Jaskirat Singh Randhawa, Kelsey Dillehay McKillip, Hirofumi Yoshino, Satoshi Kofuji, Koichi Okumura, Rand Naffouje, Matthew Koch, Xiang Ao, Kara Finley, Atsuo Sasaki; University of Cincinnati Cancer Institute, Cincinnati, OH; Department of Pathology and Labarotory Medicine, University of Cincinnati Medical Center, Cincinnati, OH; University of Cincinnati, Cincinnati, OH; Division of Biostatistics and Bioinformatics, University of Cincinnati, Cincinnati, OH; University of Cincinnati Medical Center, Cincinnati, OH; Department of Pathology and Laboratory Medicine, University of Cincinnati Medical Center, Cincinnati, OH; Weiss Memorial Hospital, Chicago, IL; Department of Pathology, University of Cincinnati, Cincinnati, OH

Background: Approximately 40% of locoregional RCC patients relapse after nephrectomy leading to lower 5 year survival rates of 53% (stage III) & 8% (metastatic). No biomarkers of prognostic significance are in clinical use at this time. It is important to identify biomarkers that can better inform clinicians the nature of disease & personalize treatment. It is even better if the biomarkers are targetable with drugs. Inosine 5''-mono-phosphate dehydrogenase type II (IMPDH2), a rate limiting enzyme in the de novo guanine nucleotide biosynthesis is upregulated in many tumor types. Work by Sasaki laboratory showed increased GTP synthesis by IMPDH2 upregulation is important for cell growth, metastasis & cell maintenance in Gliobastoma Multiforme cell lines. *Hypothesis:* We are investigating the feasibility of using IMPDH2 expression in RCC as a diagnostic & prognostic biomarker. **Methods:** 45 cases of clear cell RCC (all stages) were identified by chart review. Slides reviewed to identify blocks with carcinoma, normal tissue & interface. Tissue microarray (TMA) was constructed using the fully automated TMA Master. TMA sectioned and stained with H &E & IMPDH2 antibody. *Staining interpretation:* TMA stained with IMPDH2 were reviewed based on IRS scoring system (PP x SI) - percentage positive(PP) cells (Negative-0, *≤10% -1, ≥11%- ≤50%- 2, ≥51%-≤80% -3, and ≥81%-4) &* staining intensity (SI) (Negative-0, Weak-1, Moderate-2, and Strong-3). The scoring pathologist was blinded to the clinical data & outcomes of patients. **Results:** Preliminary results show IMPDH2 is overexpressed in RCC and tumor-normal interface compared to normal kidney. Further analyses are ongoing if IMPDH2 overexpression correlates with pertinent clinical & pathological variables including TNM stage, histologic grade (Fuhrman Grade) & oncologic outcomes including overall survival (OS) & risk of relapse. **Conclusions:** In the era of Sunitinib being approved as an adjuvant therapy (but not widely used due to lack of OS data), the above data will be important to verify if IMPDH2 can be used as a clinically useful test & may give insight to future personalized & targeted treatment strategies (IMPDH2 inhibitors like mycophenolate) for RCC.

595 Poster Session (Board #F12), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM

Disparities in survival outcomes in African Americans in renal cell carcinoma: Impact of oncological versus nononcological factors.

Margaret Frances Meagher, Aaron Bradshaw, David Anyakora, Dattatraya H Patil, Kazutaka Saito, Brittney Cotta, Yosuke Yasuda, Ahmed Eldefrawy, Stephen Ryan, Ryan Nasseri, Juliana Alksne, Fang Wan, Yasuhisa Fujii, Viraj A. Master, Ithaar Derweesh; University of California San Diego, San Diego, CA; Emory University, Atlanta, GA; Tokyo Medical and Dental University, Tokyo, Japan; Department of Urology, Tokyo Medical and Dental University, Tokyo, Japan; Winship Cancer Institute of Emory University, Atlanta, GA

Background: African-Americans have increased incidences of renal cortical tumor subtypes of lower oncological potential in the setting of lower risk disease when compared to other ethno-racial groups. However, survival outcomes are similar. We investigated the impact of African-American race on overall survival, oncological outcomes, functional outcomes, and non-cancer mortality. **Methods:** Multi-institutional retrospective analysis of patients who underwent partial or radical nephrectomy between 1998-2018. Primary outcome was overall survival (OS). Secondary outcomes included non-cancer mortality (NCM), recurrence free survival (RFS), and estimated glomerular filtration rate (eGFR) decline. Multivariable logistic regression (MVA) were used to elucidate predictive factors for OS, NCM, and RFS, and eGFR <45 and <30 ml/min/1.73m2. **Results:** 3,088 patients were divided into African American (AA, n=353) and Non-African American (NAA, n=2735) sub-groups. No difference was noted between groups with respect to mean tumor size (p=0.211) or metastases presence (p=0.846). African-American race was an independent risk factor for functional decline to eGFR<45 (OR 4.43, $p<0.001$) and eGFR<30 (OR 5.15, $p<0.001$). MVA for worsened NCM demonstrated African-American race (OR=1.72, p=0.042), increasing age (OR=1.03, p=0.001), radical nephrectomy (OR=2.98, $p<0.001$), and increasing tumor size (OR=1.26, $p<0.001$) to be independent risk factors. MVA for worsened OS included increasing age (OR=1.04, $p<0.001$), tumor size (OR=1.182, $p<0.001$), clear cell histology (OR=1.62, $p<0.001$), high tumor grade (OR=2.12, $p<0.001$), and post-operative eGFR <45 (OR=2.12, $p<0.001$). MVA for worsening RFS demonstrated high tumor grade (OR=2.38, $p<0.001$) and increasing clinical tumor size (OR=1.152, $p<0.001$) to be independent factors. **Conclusions:** African Americans undergoing renal surgery for RCC appear to have similar OS and RFS, but poorer NCM than non-African American patients. The cause of these disparities is multi-faceted and likely associated with functional decline. Nephron-sparing management should be considered in African-Americans presenting with renal cortical tumors.

596 **Poster Session (Board #F13), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM**

Association of elevated C-reactive protein with oncologic outcomes in renal CELL carcinoma: A multicenter analysis.

Sunil Hemant Patel, Margaret Frances Meagher, Kazutaka Saito, Dattatraya Patil, Ahmet Bindayi, Ahmed Eldefrawy, Stephen Ryan, Brittney Cotta, Kendrick Yim, Ryan Nasseri, Zachary Hamilton, Yosuke Yasuda, Yasuhisa Fujii, Viraj A. Master, Ithaar Derweesh; UCSD, San Diego, CA; University of California San Diego, San Diego, CA; Tokyo Medical and Dental University, Tokyo, Japan; Emory University School of Medicine, Atlanta, GA; Department of Urology, Cancer Institute Hospital of Japanese Foundation for Cancer Research, Tokyo, Japan; Winship Cancer Institute of Emory University, Atlanta, GA

Background: C-reactive protein (CRP) is a systemic inflammatory marker which has been associated with overall survival (OS) in Renal Cell Carcinoma (RCC) patients in Asia. Data supporting utility of CRP as a predictive marker in non-Asian populations are sparse and controversial. We analyzed utility of pre-treatment CRP as a predictor of survival and oncological outcomes in a multicenter cohort of RCC patients. **Methods:** Retrospective international 3 center analysis of patients of patients with RCC with pretreatment CRP values from 2006-2017. CRP $>$ 0.5mg/dl was used as threshold for elevation and the cohort was subdivided into two groups for descriptive analysis (normal-CRP $\leq$0.5 and elevated-CRP $>$ 0.5). Primary outcome was recurrence-free survival (RFS). Secondary outcome was overall survival (OS). Kaplan-Meier (KMA) and multivariable analyses (MVA) were utilized to delineate survival outcomes and their predictors. **Results:** Overall 2695 patients were analyzed (1791 Male/904 female, CRP$\leq$0.5 1198/CRP $>$ 0.5 1496; mean follow-up 36 months). Patients with elevated CRP had higher incidence of hypertension ($p = 0.001$), BMI ($p < 0.001$), and tumor size (3.91 cm vs. 6.05 cm, $p < 0.001$). MVA for RFS demonstrated elevated CRP (OR = 0.542, $p = 0.005$), increasing tumor size (OR = 0.915, $p < 0.001$), and high tumor grade (OR = 0.322 $p < 0.001$) to be independent risk factors. MVA for all-cause mortality demonstrated elevated CRP (OR = 12.396, $p = 0.005$), increasing tumor size (OR = 1.126, $p < 0.001$), high tumor grade (OR = 2.474, $p < 0.001$), and receipt of PN (OR = 1.826, $p = 0.001$) to be independent risk factors. For normal vs. elevated CRP, KMA revealed 5-year RFS of 90% vs. 85% ($p = 0.001$), 95% vs 85% ($p = 0.163$), 85% vs 62% ($p = 0.001$), 50% vs 60% ($p = 0.513$) for Stages 1, 2, 3, and 4, respectively. KMA revealed 5-year OS of 98% vs 80% ($p = 0.001$), 95% vs 80% ($p = 0.103$), 95% vs 65% ($p = 0.001$), 99% vs 40% ($p < 0.001$) for Stages 1, 2, 3, and 4, respectively. **Conclusions:** Pre-treatment CRP was an independent predictor of recurrence free survival and overall survival in a multicenter cohort of RCC patients. While further confirmation is requisite, our findings suggest incorporation of CRP into nomographic and risk stratification protocols.

597 **Poster Session (Board #F14), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM**

Development and validation of a novel scoring index (C-reactive protein, age, race, and tumor size) to predict renal functional decline post partial nephrectomy.

Margaret Frances Meagher, Dattatraya H Patil, Kazutaka Saito, Brittney Cotta, Yosuke Yasuda, Aaron Bradshaw, Ahmed Eldefrawy, Stephen Ryan, Ryan Nasseri, David Anyakora, Juliana Alksne, Fang Wan, Yasuhisa Fujii, Viraj A. Master, Ithaar Derweesh; University of California San Diego, San Diego, CA; Emory University, Atlanta, GA; Tokyo Medical and Dental University, Tokyo, Japan; Department of Urology, Tokyo Medical and Dental University, Tokyo, Japan; Winship Cancer Institute of Emory University, Atlanta, GA

Background: Functional decline is a sequelae of extirpative renal surgery with potential for significant morbidity. We utilized pre-operative patient demographics, C-reactive protein, and tumor size to design and validate a novel scoring index to predict functional decline post partial nephrectomy. **Methods:** A multi-institutional dataset was utilized for analysis of patients with pre-operative estimated glomerular filtration rate (eGFR) $>$ 60mL/min/1.73m2 by CKD-EPI equation. Multivariable analysis (MVA) was carried out for potential variables associated with development of post-operative chronic kidney disease (CKD) stage IIIB at last follow-up (eGFR $<$ 45 mL/min/1.73m2). Significant variables were included in the predictive model and assigned an index score based on odds ratio. Receiver-operating-characteristic (ROC) analysis was employed to evaluate predictive validity, and bootstrapping technique was utilized to validate the model. **Results:** 924 patients were analyzed. 826 patients had post-operative eGFR $>$ 45, while 111 patients had eGFR. Factors on MVA independently associated with increased risk of development of eGFR $<$ 45 included age 65+ (OR = 2.6, p $<$ 0.001), African-American race (OR = 2.3, p = 0.006), C-reactive protein level $>$ 0.5mg/dL (OR = 5.3, p $<$ 0.001), and tumor size $>$ 4 cm (OR = 1.458, p = 0.189). For CART (C-reactive protein, Age, Race, Tumor size) score, the following values were assigned: age ($<$ 65 = 1, age $>$ 65 = 3), race (non-African-American = 1, African-American = 2), tumor size ($<$ 4 = 1, $>$ 4cm = 2), and CRP ($<$ 0.5mg/dL = 1, $>$ 0.5mg/dL = 4). Analysis demonstrated 2.6% (12/469) of patients with a low (4-6) score had de novo eGFR $<$ 45 postoperatively, while 35% (41/117) of patients with a high (10-11) score had de novo eGFR $<$ 45. ROC analysis revealed AUC of 0.778, and ROC bootstrapping validation of 95 randomly selected patients revealed an AUC of 0.808. **Conclusions:** CART score represents a novel composite score that significantly predicts development of eGFR $<$ 45 after surgery. This scoring system may assist in patient counseling and clinical decision making, as well as an impetus to improve outcomes in at-risk patient subgroups.

598 Poster Session (Board #F15), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM

Clinical predictors of sarcomatoid kidney cancer: The results of a UCLA and french UroCCR network collaboration.

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Background: Predisposing factors for sarcomatoid dedifferentiation of renal cell carcinoma (sRCC) remain unknown. We highlighted the association of potential contributing medical conditions with the presence of sRCC. **Methods:** Patients with a renal cell carcinoma (RCC) from UCLA and the French UroCCR-45 study (only sRCC) were included in the study. Characteristics of patients with sRCC were compared with patients with RCC without sarcomatoid features (nsRCC) in univariable and multivariable logistic regression analyses. We quantified the association of age, gender, smoking status, hypertension, kidney function, and endocrine disorders: diabetes and hypothyroidism with sRCC. **Results:** A total of 2764 were included in the study (586 sRCC vs. 2178 nsRCC). On univariable analysis, age (OR=1.02, 95%CI [1.01-1.03], p<.0001), male gender (OR=1.35, 95%CI [1.10-1.65], p=.004), active smoking (OR=1.87, 95%CI [1.48-2.36], p<.0001), and diabetes (OR=1.32, 95%CI [1.03-1.70], p=.026) were associated with the presence of sRCC (Table 1). On multivariable analysis, age (+2.1% per year, OR=1.02, 95%CI [1.01-1.03], p<0.0001), male gender (OR=1.33, 95%CI [1.08-1.64], p=.008), and active smoking (OR=1.95, 95%CI [1.54-2.47], p<0.0001) were independently associated with the presence of sRCC. The AUC of the model was 0.61. **Conclusions:** In this study we found that sarcomatoid dedifferentiation was associated with age, male gender, and active smoking. Further studies are needed to confirm these findings and establish the underlying biology. Univariable logistic regression analysis of the association between potential pathogenic factors and sRCC. N=2764

Clinical Parameters	sRCC	nsRCC	Missing (%)	Odds ratio [95%CI]	p-value
Age (mean±SE, years)	62.7±0.5	60.0±0.3	0	1.02 [1.01-1.03]	**<0.0001**
Male gender (%)	72.5	66.2	0	1.35 [1.10-1.65]	**0.004**
Active smoking (%)	22.9	13.7	2	1.87 [1.48-2.36]	**<0.0001**
Diabetes (%)	17.6	13.9	1	1.32 [1.03-1.70]	**0.026**
Hypothyroidism (%)	4.2	6.0	1	0.69 [0.44-1.07]	0.09
Hypertension (%)	44.7	45.9	1	0.95 [0.79-1.15]	0.60
eGFR (mean±SE, ml/min)	69.5±1.2	69.6±0.5	12	1.00 [0.99-1.00]	0.90

599 Poster Session (Board #F16), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM

Outcomes of stereotactic ablative radiotherapy for extra-cranial oligo-metastatic renal cell cancer.

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Background: Stereotactic ablative radiotherapy (SAbR) is a standard of care for treating renal cell cancer (RCC) cranial metastasis. We describe the effect of SAbR on oligometastatic extra-cranial RCC disease course. **Methods:** We retrospectively reviewed 49 patients with oligometastatic RCC with 68 extra-cranial lesions. Patients were treated with SAbR with a curative intent from 2007 to 2017. We analyzed local control, systemic therapy free survival (mPFS), and overall survival. **Results:** With a median follow-up of 28 months (IQR: 16.0-40.3), the 1-year and 2-year overall survival after SAbR was 93.4% (95% CI: 81.0-97.8), and 83% (95% CI: 67.4-91.5) respectively. The median overall survival was not reached. The median time to systemic therapy was 13.4 months from the first SAbR(95% CI: 8.8-27.6). Median times from the first SabR course to second and third line systemic therapy (or death) were 31.8 months and 45 months, respectively. Patients in the favorable risk group by the Heng's criteria (HR = 8.67, p = 0.04), with nometastatic disease at diagnosis (HR = 10.38, $p < 0.01$) and with clear cell histology (HR = 6.15, $p < 0.01$) exhibited better survival, as shown by univariate analysis. Patients with no metastatic disease at diagnosis (HR = 2.56, p = 0.02) and only one metastasis treated with SAbR (HR = 2.36, p = 0.03) also exhibited better systemic therapy-free survival. SAbR had an excellent local control rate of 94% at 2 years with no reported grade 3 or higher toxicity. **Conclusions:** SAbR is an effective and safe treatment for oligometastatic RCC, offering excellent local control with minimal toxicity. SAbR delayed the start of systemic therapy for this RCC cohort, offering quality of life benefits for patients without adversely affecting the progression on subsequent lines of systemic therapy. These findings call for prospective verification.

600 **Poster Session (Board #F17), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM**

Pembrolizumab (pembro) and cabozantinib (cabo) in patients (pts) with metastatic renal cell carcinoma (mRCC): Phase I results.

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Background: PD-L1- and VEGF-targeted therapies have improved survival for mRCC pts and mechanisms of synergy have been reported. We conducted a phase I/II study to evaluate the safety and efficacy of pembro and cabo in mRCC pts. Phase I data are presented here. **Methods:** mRCC pts received pembro and cabo in a standard 3+3 dose escalation to determine the dose limiting toxicity (DLT), maximum tolerated dose (MTD), and objective response rate (ORR). Cabo was dosed at 40mg QD and 60mg QD in the first and second cohorts, respectively. Pembro was dosed at 200mg IV Q3W in all cohorts. The DLT window was 21 days. Scans were obtained every 9 weeks. Treatment beyond progression was allowed. **Results:** Eight pts (6M, 2F) were enrolled in the dose escalation cohort with cabo 40mg (5 pts) or 60mg (3 pts) and pembro 200mg. Two pts were not evaluable for DLT due to missing ≥25% of the planned cabo doses in C1, not related to DLT. Median age was 52.5 yrs (range 40-68). Seven pts had clear cell RCC and 1 pt had non-clear cell RCC. Seven pts had MSKCC intermediate risk and 1 pt had MSKCC poor risk. All pts had prior nephrectomy. Median number of prior therapies was one (range 1-3). No DLTs were observed. Drug-related G1 and G2 adverse effects included fatigue (87.5%), weight loss (75%), anorexia (50%), diarrhea (50%), dysgeusia (50%), and abnormal LFTs (50%). One pt had SAE of G3 reversible posterior leukoencephalopathy syndrome during C4, attributed to cabo. One pt each developed G3 hypertension, G3 anorexia, and G3 confusion, all occurring outside the DLT window. No dose reductions were needed at the 40mg cohort. One pt in the 60mg cohort required dose reduction to 40mg after C5. All patients were evaluable for response: 2 PR (at 60 mg cohort), 5 SD [median duration SD 18 wks (range 9-36+)], 1 PD; ORR 25%; clinical benefit rate 87.5%. No correlation was seen between PD-L1 status (archival tissue) and response. **Conclusions:** The MTD was determined to be pembro 200 mg Q3W and cabo 60 QD. Enrollment in the phase II dose expansion is ongoing and the MTD may be adjusted based on additional pt experience and long-term tolerability. There was encouraging early efficacy. This is an investigator-initiated study sponsored by Merck. Clinical trial information: NCT03149822.

601 Poster Session (Board #F18), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM

The prognostic value of glycosylphosphatidylinositol-anchored 80 kD protein (GPI-80) positive myeloid derived suppressor cells (MDSCs) in peripheral blood of metastatic renal cell carcinoma (mRCC) patients.

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Background: Myeloid derived suppressor cells (MDSCs) are found to play essential roles in various tumors and to associate with the prognosis of patients. However, the prognostic values of MDSCs in metastatic renal cell cancer (mRCC) are still undefined. Glycosylphosphatidylinositol-anchored 80 kD protein (GPI-80) is known as a regulator of Mac-1 (CD11b/CD18) and closely related with differentiation of myeloid cells. The object of our study was to interrogate the association of MDSCs in peripheral blood with clinical outcomes of mRCC patients by using GPI-80. **Methods:** Peripheral blood samples, collected from 23 mRCC patients before treatment and 16 healthy volunteers, were stained with several myeloid cell antigens such as CD16, CD15, CD33, and GPI-80 to mark neutrophils and monocytes. We measured the expression levels (mean of florescence intensity, MFI) and deviation (coefficient variation, CV) of myeloid antigens by flow cytometry. To investigate the immunosuppressive function of GPI-80 positive cells, reactive oxygen species (ROS) and LAP-1 (precursor of TGF-β1) were measured. The impact of the cell surface antigens on overall survival (OS) was evaluated using the univariate and multivariate Cox regression analysis. **Results:** The MFI or CV of GPI-80 on neutrophilic or monocytic cells were significantly difference in between patients and healthy volunteers. LAP-1 expression and ROS production in monocytic cells were increased in patients than in healthy volunteers, and correlated with expression of GPI-80 MFI ($p = 0.0107$ and $p = 0.0381$, respectively). Regarding the prognostic values, both GPI-80 CV of neutrophilic cells and GPI-80 MFI of monocytic cells were associated with poor OS of mRCC patients ($p < 0.01$). Multivariate analysis showed that GPI-80 MFI of monocytic cells were independent unfavorable prognosis marker (HR 2.427, $p = 0.044$). **Conclusions:** These results showed that change of GPI-80 expression on myeloid cells in peripheral blood representing appearance of MDSCs was likely to be negative predictors in patients with mRCC.

602 Poster Session (Board #F19), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM

Comparison of retroperitoneal and transperitoneal robotic partial nephrectomy by pentafecta perioperative and renal functional outcomes.

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Background: To compare and analyze surgical, oncological and functional outcomes of transperitoneal (TRPN) and retroperitoneal robotic partial nephrectomy (RRPN). **Methods:** Out of 566 consecutive patients who underwent RAPN by a single surgeon from December 2008 to July 2017, this study included 523 patients (TRPN 310, RRPN 213) who evaluated preoperative and 1-year postoperative estimated glomerular filtration rate (eGFR). Our primary endpoint was to compare the perioperative and postoperative outcomes of both approaches by the measure of Pentafecta (negative surgical margin, no 30-day complication, warm ischemic time (WIT) $\leq$25 minutes, return of estimated glomerular filtration rate (eGFR) to $>$ 90% from baseline and no upstaging of chronic kidney disease). Secondary endpoint was to find the factors associated with Pentafecta by multivariate regression analysis. **Results:** No significant difference was found in terms of age, BMI, laterality, history of hypertension or diabetes, ASA grade, tumor size and RENAL nephrometry score. These outcomes were lower in the RRPN group: operative time [median (IQR) 244 (202-295) vs. 273 (230-314); $p < 0.001$], WIT [median (IQR) 19 (15-25) vs. 21 (16-27); $p < 0.008$] and estimated blood loss (EBL) [median (IQR) 100 (60-200) vs. 150 (100-200); $p < 0.003$]. Hospital stay, baseline eGFR, 1-year postoperative eGFR, the rate of Pentafecta achievement, recurrence and complications were not different. The rate of WIT $\leq$ 25 minutes was solely significantly different (TRPN 69.7% vs. RRPN 77.9%, $p = 0.045$) in the Pentafecta criteria. Multivariate analysis revealed tumor size [OR (95% CI) 0.641 (0.536-0.767), $p < 0.001$) and hospital stays (OR 0.639, $p < 0.001$) as predictive for lack of Pentafecta. **Conclusions:** RRPN demonstrated less operative time, WIT and EBL than TPRN. Pentafecta achievements were equivalent in both approaches. Tumor size and hospital stays were found as predictive factors of Pentafecta.

603 Poster Session (Board #F20), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM

Prognostic role of PD-L1 expression in patients with advanced renal cell carcinoma (RCC) treated with sunitinib.

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Background: the prognosis and treatment of advanced RCC has improved over the last decade due to a number of effective anti-angiogenic and immune checkpoint inhibitors (ICPI) therapies. Certain clinical factors, such as low Karnofsky status ($\leq$ 70%); less than a one year period from diagnosis to treatment administration**;** low serum hemoglobin; high corrected serum calcium; high lactate dehydrogenase; elevated neutrophil count or platelet count exceeding the upper limit of the normal range, have been able to stratify patients into three distinct prognostic groups: favorable (zero risk factors), intermediate (one to two), and poor risk (more than two). Nowadays, the relationship between PD-L1 expression with treatment response and the survival rate of RCC is a current topic of interest. **Methods:** a retrospective analysis of 182 patients with advanced RCC who received sunitinb in a single Institution has been conducted with the aim of analyzing PD-L1 as a prognostic factor. To carry out the immunohistochemical analysis, microscopy samples have been treated with the *PD-L1 IHC 22C3 pharmDx* assay, which is intended to measure the percentage of PD-L1 expression in the primary tumor tissue. **Results:** a total of 65 patients with primary tumor tissue sampling, who were never treated with (ICPI), were analyzed. Among these, 95% were considered as intermediate or poor risk and 47% had PD-L1 expression. The results have shown that PD-L1 expression is associated with worse progression-free survival (PFS) and overall survival (OS). In patients with no expression of PD-L1, the median PFS was 16.89 months (95% confidence interval 11.0 – 40.87 months) and 12.61 months for those with some % of PD-L1 expression (4.43 – 53.09). (χ^2 = 1.16; Pr > χ^2 = 0.20). Likewise, the median OS was 42.28 months (13.76 – 68.13) for patients with no expression of PD-L1 and 24.60 months for those with some % of PD-L1 expression (13.76- not reached) (χ^2 = 0.12; Pr > χ^2 = 0.73). **Conclusions:** patients treated with sunitinib who express PD-L1, have shown shorter PFS and OS. Its validation as an independent prognostic factor, with regard to other standard clinical parameters, must be considered in order to develop a more tailored approach to treatment decision.

604 Poster Session (Board #F21), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM

Postoperative long-term prognosis of localized renal cell carcinoma after partial or radical nephrectomy: Analysis of cancer metastasis and deaths during a more than five-year follow-up.

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Background: We performed a long-term follow-up study to evaluate the survival and metastatic outcomes of non-metastatic renal cell carcinoma (RCC) after curative removal of tumor. **Methods:** We retrospectively reviewed the clinical and pathological features of 5434 patients with localized renal cell carcinoma admitted to five Korean tertiary-care institutions between 2000 and 2012, who had undergone curative surgeries with partial or radical nephrectomy with/without lymph nodal dissection. The patients below the age of 19 years (N=9) with benign histology (N=24), and with no follow-up records (N=540) were excluded. A total of 4861 patients, followed-up for at least 1 year after the surgery, were enrolled finally. The deaths were defined as intraoperative, post-operative or RCC-related deaths. We analyzed the metastasis-free survival, cancer-specific survival, and overall survival outcomes according to the pathological stages. **Results:** The median age of patients at the time of surgery, male-to-female ratios, median follow-up duration, overall survival and metastasis-free survival times were 56 years (range: 19-94 years), 3471/1390 (71.4%/ 28.6%), 33.7 months (range: 12-297 months), 175.1 months (12-297.1 months), and 61 months (range: 12-94 months), respectively. A total of 518 (10.7%) deaths, including 338 (7.0%) RCC-related death and 164 (3.3%) deaths related to other causes were reported. Metastasis and recurrences were observed in 140 (2.9%) and 462 (9.5%) patients, respectively. The respective pathologic T1/2/3/4/x and N1 stages, namely, 3757/389/644/57/6 (77.3/8.0/13.3/1.2/0.1%) and 133 (2.7%) were observed. The rates of histological types of clear cell papillary/ chromophobe/ collecting duct/ unclassified/ MLCRCCLMP/ mixed cell papillary/ unknown were 83.4%/ 1.5%/ 7.1%/ 0.4%/ 1.1%/ 0.5%/ 0.2%/ 0.3%/ 0.1%/ 5.3%. The 10-year metastasis-free survival rate was 86.0% including 100%, 91.0%, 64.1%, and 11.8% incidence for stages I, II, III, and IV, respectively. **Conclusions:** The long-term survival was seen among patients who underwent nephrectomy for non-metastatic renal cell carcinoma.

605 Poster Session (Board #F22), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM

Patterns of response of organ specific metastasis in patients with metastatic renal cell cancer (mRCC) treated with an immune checkpoint inhibitor (CPI) post tyrosine kinase inhibitor (TKI).

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Background: Both TKIs and the novel immune CPIs targeting PD/PDL1 are now standard treatments for patients with mRCC. Mixed responses in metastatic lesions have been observed. We examined organ specific radiologic responses in a cohort of patients with mRCC who were initially treated with TKI followed by CPI. **Methods:** We identified patients who were treated with first line TKI followed by CPI from a prospectively maintained database of all mRCC patients treated at our institution from 2010 to 2018. We examined best response to TKI and CPI, as well as organ specific responses to TKI and CPI. Statistical analysis was performed using odds ratios and Fishers exact test. **Results:** We identified 31 patients with evaluable disease who were treated with a TKI followed by CPI. Best responses to TKI were partial response (PR) (n = 7), stable disease (SD) (n = 17) and progressive disease (PD) (n = 6). Of TKI responders, 4 had lesions in $\geq$2 organs respond and 3 had a lesion in a single organ respond. Of the 3 patients who responded to CPI, all had lesions in $\geq$2 organs respond. Patients who had PD to TKI did not respond to CPI. Organ specific metastases at time of initiation of TKI and CPI are described in the table. In lung lesions, the odds of a response to CPI with or without an initial response to TKI were 0.16 and 0.57 respectively (OR 0.29, p = 0.595). In lymph node (LN) metastases, the odds of a response to CPI with or without an initial response to TKI were 0.16 and 0.62 respectively (OR 0.27, p = 0.354). Two patients had a response to TKI in the liver but none had a response to subsequent CPI. Of 3 patients who had a response to TKI in the renal primary, 1 had a response to CPI. **Conclusions:** In this small series, these data suggest that first line TKI response may dictate subsequent CPI response in an organ specific manner, with higher numbers of CPI responses in lung and LN metastases in patients who did not have TKI response in these organs. This may be due to immune modulation by prior TKI or to tumor heterogeneity. Studies are needed to further elucidate this phenomenon.

	TKI [no. (%)]	IO [no. (%)]
Lung	18 (55)	20 (65)
LN	20 (65)	26 (84)
Liver	8 (26)	12 (39)
Kidney	4 (13)	4 (13)

606 Poster Session (Board #G1), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM

Real-world experience with sunitinib treatment in patients with metastatic renal cell carcinoma: Clinical outcome according to risk score.

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Background: ADONIS, an ongoing, observational study in 9 EU countries, evaluates treatment patterns/outcomes in patients (pts) with metastatic renal cell carcinoma treated with 1st-line (1L) sunitinib (SU) and/or 2nd-line (2L) axitinib (AX) post SU. Analysis of the data is planned in 4 parts, to occur stepwise as data matures; evaluation of SU efficacy in intermediate (INT) risk pts is presented here. Future analyses include sequencing data, SU followed by AX and other treatments (cabozantinib, nivolumab and others); SU and AX therapy management strategies, and quality of life. **Methods:** Pts enroll at start of 1L SU or 2L AX post SU. Data cutoff: May 31, 2018. Analysis focused on 1L SU. **Results:** 467 pts, median age 64 y (range 31–90), 77.7% were male, with ECOG PS $<$ 2 = 90.2% and ECOG PS $\geq$ 2 = 9.8% at SU initiation. Overall median progression-free survival (mPFS) was 10.4 mo (95% CI 9.3–12.5), and median overall survival (mOS) 34.0 mo (95% CI 28.3–46.6). Data on individual risk factors (RF) were available for 120 pts, allowing analysis by INT 1RF and INT 2RF groups for this subset. Clinical trial information: NCT02184416. **Conclusions:** For pts overall and by risk group stratification, survival estimates were aligned with improvements in clinical practice over the past decade. In pts with INT risk with 1RF, OS was very similar to pts with good risk. However further exploration is needed to confirm these observations.

Outcome for 1L SU Treated Patients: By IMDC risk group (n=238)*

IMDC	Good n=73 (15.7%)	INT n=117 (25.2%)	Poor n=48 (10.3%)
mPFS, mo (95% CI)	23.8 (16.5-28.5)	11.8 (8.1-17.4)	4.6 (2.5-7.7)
mOS, mo (95% CI)	97.1 (46.3-NE)	33.5 (20.5-46.6)	10.0 (4.5-19.8)

By IMDC Individual RF at SU start (n=120)				
Calculated IMDC	Good	INT 1RF	INT 2RF	Poor
	n=22 (18.3%)	n=28 (23.3%)	n=17 (14.2%)	n=53 (44.2%)
mPFS, mo (95% CI)	16.5 (8.7-18.9)	9.0 (6.3-NE)	4.6 (2.5-10.7)	2.7 (2.4-3.4)
mOS, mo (95% CI)	21.6 (16.3-NE)	20.5 (15.5-NE)	15.1 (4.1-NE)	8.7 (4.9-12.3)

* Risk classification was not provided by investigators for 226 pts (48.7%). CI=confidence interval; IMDC=International Metastatic Renal Cell Carcinoma Database; NE=not evaluable.

607 **Poster Session (Board #G2), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM**

Evaluation of tumor microenvironment and biomarkers of immune checkpoint inhibitor (ICI) response in metastatic renal cell carcinoma (mRCC).

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Background: ICIs are now standard of care for mRCC; however, there are few biomarkers to predict ICI response. Recent data from atezolizumab/bevacizumab trials in mRCC suggest tumors with high T_{eff}^{high}/PD-L1+ are more likely to respond to ICI. Here, we use this T_{eff} gene panel as well as other markers of inflammation in the tumor microenvironment to correlate with ICI responses. **Methods:** This multicenter study evaluated 69 pts with mRCC treated with ICIs. FFPE tumor samples were evaluated by RNA sequencing to measure transcript levels of genes related T_{eff} status. T_{eff} status was defined as the mRNA expression of 17 genes (CD8, CD27, IFNG, GZMA, GZMB, PRF1, EOMES, CXCL9, CXCL10, CXCL11, CD274, CTLA4, FOXP3, TIGIT, IDO1, PSMB9, TAP1), with $T_{eff}^{high/low}$ separated at the median. PD-L1 positivity was defined as $\geq$1% TPS based on Dako 22C3 IHC assay, and TMB high as $>$ 10 mutations per megabase. Inflamed tumors were defined as CD8 expression in the top 75th percentile compared to a large reference population of multiple tumor types. Best responses to ICI was determined by an expert radiologist using RECIST 1.1 criteria. Inflamed tumor status, T_{eff} gene expression, PD-L1 positive, and TMB were associated with disease control (DC, defined as CR, PR, or stable disease). DC comparisons were tested using a chi-squared test with Yates's continuity correction. **Results:** DC was 63% (5/8) amongst PD-L1 positive pts and 52% (31/60) in PD-L1 negative patients (p = 0.84). Only 2 pts were TMB high. The majority of mRCC tumors (97%, 67/69) were TMB low. 6-month DC in TMB high tumors was 50% (1/2) and 49.3% (33/67) in TMB low tumors (p = 1.0). 36 pts were classified as T_{eff}^{high} and 33 patients were classified as T_{eff}^{low}. 6-month DC was 61% (22/36) in the T_{eff}^{high} cohort and 36% (12/33) in the T_{eff}^{low} cohort (p = 0.069). 6-month DC was 64% of inflamed tumors (16/25) vs 41% of non-inflamed tumors (18/44) (p = 0.111). **Conclusions:** TMB high and PD-L1 expression do not reliably predict for DC in pts with mRCC. Utilizing a gene signature score may better predict ICI response.

608 **Poster Session (Board #G3), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM**

The association of rising serum uric acid levels with survival in renal cell carcinoma.

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Background: To investigate the association of serum uric acid (SUA) levels along with statin use in Renal Cell Carcinoma (RCC), as statins may be associated with improved outcomes in RCC and SUA elevation is associated with increased risk of chronic kidney disease (CKD). **Methods:** Retrospective study of patients undergoing surgery for RCC with preoperative and postoperative SUA levels between 8/2005-8/2014. Increased SUA was defined as $>$ 7mg/dL for males and $>$ 5.7 mg/dL for females. Analysis was carried out between patients with increased postoperative SUA vs. patients with decreased/stable postoperative SUA. Kaplan-Meier analysis (KMA) calculated overall survival (OS). Multivariable analysis (MVA) was performed to identify factors associated with increased SUA levels and all-cause mortality. **Results:** 905 patients were analyzed. Decreased/stable SUA levels were noted in 675(74.6%) and increased SUA levels were noted in 230(25.4%). A higher proportion of patients with decreased/stable SUA levels took statins (27.9% vs 18.3%, p = 0.004). Increased SUA had significantly greater de novo CKD (38.7% vs. 18.4%, p $<$ 0.001) and proteinuria (30.9% vs. 20.7%, p = 0.002). KMA demonstrated improved 5-year OS for patients with decreased/stable SUA compared to increased SUA for stage I, (93% vs. 60%), stage II (87% vs. 50%), and stage III (88% vs. 62%) RCC (all p $<$ 0.001). MVA revealed that increasing BMI (OR 1.05, p = 0.009), statin use (OR 0.11, p $<$ 0.001), dyslipidemia (OR 2.66, p = 0.004), stage III/IV cancer (OR 1.89, p = 0.015 and OR = 10.78, p $<$ 0.001), and postoperative de novo CKD stage 3 (OR 5.95, p $<$ 0.001) were predictors for increased postoperative SUA levels. MVA revealed increasing BMI (OR 1.09, p = 0.002), increasing SUA (OR = 4.70, p $<$ 0.001), stage IV RCC (OR = 7.7, p $<$ 0.001, and de novo CKD stage 3 (OR 7.07, p $<$ 0.001) to be independent risk factors for worsened all-cause mortality. **Conclusions:** Increasing SUA post operatively was associated with worsened outcomes in RCC patients. Decreased SUA levels were associated with statin intake and lower stage disease as well as lack of progression to CKD and anemia. Further investigation is requisite.

609 **Poster Session (Board #G4), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM**

The association between hospitals' risk-adjusted emergency department visits and survival and costs in kidney cancer patients.

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Background: As payers turn to alternative payment models, including the CMS Oncology Care Model, risk-adjusted emergency department (ED) visits are being incorporated as a quality. Yet little is know about this metric compares to existing metrics such as risk-adjusted mortality rates and costs. **Methods:** Using 2007-2012 SEER-Medicare data, we used logistic regression to model occurrence of an ED visit within 30 and 365 days for all kidney cancer patients receiving initial surgery. Our model controlled for demographics, stage, histology, systemic targeted therapy, and comorbidities. Based on model predictions, we created a ratio of actual versus predicted ED visits for hospitals to identify hospitals with higher and lower than predicted ED visit rates. We estimated the association between the hospitals' ED visit ratio and hospitals' risk-adjusted 365-day mortality rates, and 6- and 12-month total costs and total costs (less ED visits). **Results:** In our sample of 6,078 patients, 15.5% had an ED visit within 30 days of surgery and 43.5% within 365 days. For hospitals with $\geq$10 patients, we found no statistically significant association between 30-day or 365-day risk-adjusted ED visit rate and their 365-day risk-adjusted mortality rate. While hospitals' 30-day ED visit rates were significantly associated with 6- and 12-month costs, the association was largely driven by the cost of the ED visit itself. Conversely, hospitals' 365-day ED visit rates were significantly associated with 12-month costs after excluding the cost of the ED visit. **Conclusions:** Our results suggest hospitals' risk-adjusted ED visit rates capture a qualitatively different measure of quality than the more commonly reported mortality rates and is significantly associated with patient cost.

610 Poster Session (Board #G5), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM

Real-world assessment of clinical outcomes among first-line (1L) sunitinib (SUN) patients (pts) with metastatic renal cell carcinoma (mRCC) by the international mRCC database consortium (IMDC) risk group.

Marie-France Savard, J Connor Wells, Jeffrey Graham, John A. Steinharter, Bradley Alexander McGregor, Frede Donskov, Georg A. Bjarnason, Ulka N. Vaishampayan, Aaron Richard Hansen, Marco Adelmo James Iafolla, Giovanni Zanotti, Lynn Huynh, Mei Sheng Duh, Daniel Yick Chin Heng; University of Calgary, Calgary, AB, Canada; Dana-Farber Cancer Institute, Boston, MA; Aarhus University Hospital, Aarhus, Denmark; Sunnybrook Health Sciences Centre, Toronto, ON, Canada; Karmanos Cancer Institute, Detroit, MI; Princess Margaret Cancer Centre, Toronto, ON, Canada; Pfizer Inc., New York, NY; Analysis Group, Inc., Boston, MA

Background: Prognostic factors such as the IMDC criteria have included all types of targeted therapy. This study assesses clinical outcomes and provide benchmarks for mRCC pts treated specifically with 1L SUN in the real world to provide contemporary benchmarks for outcomes and survival. **Methods:** Clear cell mRCC pts initiating SUN as 1L therapy between 2010-2018 were included in a retrospective database study. Kaplan Meier analysis was used to estimate median time to treatment discontinuation (TTD) and overall survival (OS: time to death) by IMDC risk groups based on Karnofsky Performance Status $<$ 80%, diagnosis to treatment interval $<$ 1 year, anemia, neutrophilia, hypercalcemia and thrombocytosis. **Results:** Among 1,769 1L SUN pts with clear cell in the RW clinical database, 318 (18%) had favorable, 1,031 (58%) had intermediate and 420 (24%) had poor IMDC risk. Across the favorable, intermediate, and poor risk groups, pts had similar mean age in years, gender distribution, and year of SUN initiation (age: 63.8, 62.9 and 62.6; male: 74%, 75%, and 72%; SUN initiation year of 2010-2013: all 71%). In the favorable risk group, 99% received nephrectomy vs 88% in intermediate and 66% in poor risk group. Median TTD was 15.0, 8.5, and 4.2 months (mos) in the favorable, intermediate, and poor risk groups, respectively, and was 7.1 mos in the combined intermediate/poor risk groups. Median OS was 52.1, 31.5, and 9.8 mos in the favorable, intermediate, and poor risk groups, respectively, and was 23.2 mos in the combined intermediate/poor risk groups. **Conclusions:** This real world study based on a contemporary cohort of 1L SUN mRCC pts found a median OS of 52 mos which sets a new benchmark for clear cell mRCC in the favorable risk group. OS in the intermediate and poor risk groups are similar to previous reports. This affects pt counselling and clinical trial design.

611 **Poster Session (Board #G6), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM**

PAzopanib as first line in MEtastatic RCC patients: A "real-world" ITalian experience (PAMERIT study)—Preliminary results.

Alessandra Mosca, Ugo De Giorgi, Giuseppe Procopio, Umberto Basso, Giacomo Carteni, Sebastiano Buti, Emanuele Naglieri, Luca Galli, Orazio Caffo, Giuseppe Fornarini, Francesco Boccardo, Gaetano Facchini, Franco Morelli, Paolo Andrea Zucali, Claudia Caserta, Giuseppe Di Lucca, Zuzana Sirotova, Alessandra Gennari, Paolo Bruzzi, Camillo Porta; Oncology, Maggiore Della Carita University Hospital, Novara, Italy; Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori (IRST) IRCCS, Meldola, Italy; Medical Oncology Department, Fondazione IRCCS Istituto Nazionale dei Tumori di Milano, Milan, Italy; Istituto Oncologico Veneto IOV - IRCCS, Padova, Italy; A.O.R.N. Antonio Cardarelli di Napoli, Napoli, Italy; Medical Oncology Unit, University Hospital of Parma, Parma, Italy; National Cancer Centre, Istituto Tumori Giovanni Paolo II, Bari, Italy; Azienda Ospedaliero-Universitaria Pisana, Istituto Toscano Tumori, Pisa, Italy; Santa Chiara Hospital, Trento, Italy; San Martino Hospital, Genova, Italy; Academic Unit of Medical Oncology, IRCCS San Martino University Hospital - IST National Cancer Research Institute, Genoa, Italy; Istituto Nazionale Tumori Fondazione G. Pascale - IRCCS, Naples, Italy; IRCCS Casa Sollievo della Sofferenza, San Giovanni Rotondo, San Giovanni Rotondo, Italy; Humanitas Cancer Center, Humanitas Clinical and Research Center, Rozzano, Italy; Medical Oncology, Terni, Italy; Ospedale Civile Di Saronno, Lissone, Italy; Oncology and Onco-hematology, Regional Hospital Parini, Aosta, Italy; University of Eastern Piedmont, Novara, Italy; IRCCS Azienda Ospedaliera Universitaria San Martino – Ist - Istituto Nazionale Per La Ricerca Sul Cancro, Genoa, Italy; Department of Internal Medicine, University of Pavia and Division of Traslational Oncology, IRCCS Istituti Clinici Scientifici Maugeri, Pavia, Italy

Background: Pazopanib (Pazo) became a standard of care in metastatic renal cell cancer (mRCC) patients (pts) based on 2 prospective trials, but "real life" data are slight. **Methods:** We retrospectively analyzed clinical outcomes in a large series of mRCC pts routinely treated with 1st line Pazo, among 39 Italian Centers. Descriptive statistics has been performed using Chi-Square and Pearson rank correlation test. Progression-free survival (PFS), overall survival (OS) and safety data are still under investigation. **Results:** 474 mRCC pts have been collected and divided in 4 age categories: 1) ≤50 yrs old (9.4%); 2) 51-64 yrs old (32.6%); 3) 65-74 yrs old (33.0%); 4) ≥75 yrs old (25.0%). According to Heng score, 25.6%, 48.4% and 10.4% pts had good, intermediate and poor prognosis, respectively, without correlations with age (p = 0.128). Clear cell was the most represented histology (87.3%), independently from age (p = 0.556). 84.6% pts underwent nephrectomy, mainly younger pts (p = 0.000). Pazo initial daily dose was 800 mg in 76.5% pts, 600 mg in 10.8% pts and 400 mg in 12.7% pts, with a significant dose reduction in elderly pts: Pazo 800 was administered in 86.7% of ≤50 yrs old pts and in 54.2% of ≥75 yrs old pts (p = 0.000). Complete (CR)/partial response (PR), stable and progressive disease have been recorded in 37%, 39.5% and 23.5% pts, respectively. Radiological response directly correlated either with age (CR/PR in 55.6% of ≤50 yrs old pts vs 28.8% of ≥75 yrs old pts; p = 0.009) and with Heng score (CR/PR in 47.1% of good prognosis pts vs 24.5% of poor prognosis pts; p = 0.002). **Conclusions:** "Real world" data showed that younger (≤50 yrs old) mRCC pts more frequently underwent nephrectomy, received Pazo 800 mg daily and obtained CR/PR, with respect to elderly pts (≥75 yrs old). CR/PR to Pazo is associated with good prognosis. PFS and OS will be provided.

612 Poster Session (Board #G7), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM

Association of inflammation and clinical outcomes (CO) in metastatic renal cell carcinoma (mRCC) patients (pts) treated with cabozantinib (cabo).

Dylan J Martini, Julie M. Shabto, Yuan Liu, Bradley Curtis Carthon, Alexandra Speak, Elise Hitron, Greta Russler, Sarah Caulfield, Kenneth Ogan, Wayne Harris, Omer Kucuk, Viraj A. Master, Mehmet Asim Bilen; Department of Hematology and Medical Oncology, Emory University School of Medicine, Atlanta, GA; Departments of Biostatistics and Bioinformatics, Emory University, Atlanta, GA; Winship Cancer Institute of Emory University, Atlanta, GA; Department of Pharmaceutical Services, Emory University School of Medicine, Atlanta, GA; Department of Urology, Emory University School of Medicine, Atlanta, GA

Background: Ratios of neutrophils, monocytes, and platelets to lymphocytes (NLR, MLR, and PLR) are associated with poor CO in cancer pts. We investigated the association of NLR, MLR, and PLR and CO in mRCC pts treated with cabo. **Methods:** We performed a retrospective study of 65 mRCC pts treated with cabo at Winship Cancer Institute from 2016-2018. Overall survival (OS) and progression free survival (PFS) were calculated from first dose to date of death and radiographic or clinical progression, respectively. NLR, MLR, and PLR were obtained at baseline (BL) and 6 (±2) weeks (6W) after cabo initiation. Optimal cut (OC) was determined searching all cuts and testing them by bias adjusted log rank test to associate with PFS. Multivariate analysis (MVA) was performed using Cox proportional hazard model. **Results:** The medians were: 2.8 (NLR), 0.4 (MLR), and 176.7 (PLR). Increased NLR, MLR, and PLR were significantly associated with worse CO (Table). **Conclusions:** High NLR, MLR, and PLR may be poor prognostic factors in mRCC pts treated with cabo. Larger studies are needed to validate the results of this study.

Association between NLR, MLR, and PLR and CO.

			UVA				MVA†			
			OS		PFS		OS		PFS	
Variable	Time Point	Relation to OC	HR (CI)	p-value	HR (CI)	p-value	HR (CI)	p-value	HR (CI)	p-value
NLR	BL	Above vs Below (n=25 vs 37)	2.52 (1.18-5.36)	**0.016***	2.41 (1.32-4.40)	**0.004***	2.71 (1.04-7.11)	**0.042***	2.72 (1.29-5.73)	**0.009***
	6W	Above vs Below (n=12 vs 45)	3.86 (1.63-9.14)	**0.002***	4.85 (2.33-10.11)	**<0.001***	2.29 (0.80-6.56)	**0.121**	4.53 (1.69-12.15)	**0.003***
MLR	BL	Above vs Below (n=16 vs 46)	3.04 (1.44-6.41)	**0.004***	3.32 (1.79-6.16)	**<0.001***	3.56 (1.35-9.42)	**0.011***	4.39 (1.97-9.77)	**<0.001***
	6W	Above vs Below (n=25 vs 32)	1.77 (0.82-3.84)	0.149	2.35 (1.24-4.45)	**0.009***	1.82 (0.68-4.90)	0.235	2.46 (1.16-5.23)	**0.020***
PLR	BL	Above vs Below (n=30 vs 32)	2.23 (1.03-4.83)	**0.042***	2.23 (1.19-4.15)	**0.012***	1.95 (0.80-4.78)	0.142	1.78 (0.90-3.53)	0.097
	6W	Above vs Below (n=31 vs 26)	3.86 (1.60-9.33)	**0.003***	3.00 (1.53-5.86)	**0.001***	3.43 (1.14-10.34)	**0.028***	2.23 (1.02-4.87)	**0.045***

†MVA controlled for gender, race, IMDC risk group, # of metastatic sites, age, and ccRCC
*statistical significance at alpha < 0.05

613 Poster Session (Board #G8), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM

Body mass index (BMI) and toxicities and association with clinical outcomes (CO) in metastatic renal cell carcinoma (mRCC) patients (pts) treated with cabozantinib (cabo).

Dylan J Martini, Julie M. Shabto, Yuan Liu, Bradley Curtis Carthon, Alexandra Speak, Elise Hitron, Greta Russler, Sarah Caulfield, Kenneth Ogan, Wayne Harris, Viraj A. Master, Omer Kucuk, Mehmet Asim Bilen; Department of Hematology and Medical Oncology, Emory University School of Medicine, Atlanta, GA; Departments of Biostatistics and Bioinformatics, Emory University, Atlanta, GA; Emory University Winship Cancer Institute, Atlanta, GA; Winship Cancer Institute of Emory University, Atlanta, GA; Department of Pharmaceutical Services, Emory University School of Medicine, Atlanta, GA; Department of Urology, Emory University School of Medicine, Atlanta, GA

Background: BMI has been explored as a prognostic factor in cancer pts and treatment-related toxicities have been associated with responses to VEGF-targeted therapy in mRCC pts. We investigated the association of BMI and adverse events (AEs) and CO in mRCC pts treated with cabo. **Methods:** A retrospective analysis of 65 pts with mRCC treated with cabo at Winship Cancer Institute from 2016 to 2018 was performed. Overall survival (OS), progression-free survival (PFS), and objective response (OR) were used to measure CO. OS and PFS were calculated from first cabo dose to death and radiographic or clinical progression, respectively. An OR was defined as a partial response (PR) or a complete response (CR) using RECISTv1.1. BMI was collected at baseline (BL) and 6 ($\pm$2) weeks after cabo initiation. AEs were obtained from clinic notes. Univariate analysis (UVA) of association between BMI and CO was carried out using logistic regression model for OR and proportional hazard model for OS and PFS. **Results:** The median age was 63 years and 26% were African American. The majority were either IMDC intermediate or poor-risk (59% and 34%, respectively). Most pts (67%) had a BMI $\geq$ 25 and the median BMI at BL was 26.6. There was no difference in incidence of AEs between pts with BMI $<$ 25 and pts with BMI $\geq$ 25. Gastrointestinal (GI) AEs incidence was also comparable among pts with a BMI $\geq$ 25 (62%) and pts with BMI $<$ 25 (57%, p = 0.666). Increased BMI at 6W was significantly associated with prolonged OS and increased baseline BMI at BL showed a trend towards longer OS (Table). **Conclusions:** Increased BMI may be associated with improved CO in mRCC pts treated with cabo, but there may not be a difference in AEs based on BMI. Larger analyses are needed to validate these findings.

UVA of association between BMI and CO.

		OS		PFS		OR*	
Variable	**Time Point**	**HR (CI)**	**p-value**	**HR (CI)**	**p-value**	**OR** (CI)**	**p-value**
BMI	BL Median: 26.6	0.94 (0.87-1.01)	0.073	0.98 (0.94-1.03)	0.489	0.99 (0.90-1.08)	0.774
	6W Median: 25.8	0.90 (0.83-0.98)	**0.016*** **	0.97 (0.92-1.03)	0.298	-	-

*Objective response: probability of PR+CR were modeled. **odds ratio ***statistical significance at alpha $<$ 0.05

614 **Poster Session (Board #G9), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM**

Angiogenic and immunomodulatory biomarkers in axitinib-treated patients (pts) with advanced renal cell carcinoma (aRCC).

Brian I. Rini, Bernard Escudier, Danielle Murphy, Panpan Wang, Jamal Christo Tarazi, Robert J. Motzer; Cleveland Clinic Taussig Cancer Institute, Cleveland, OH; Medical Oncology, Gustave Roussy, Université Paris-Saclay, Villejuif, France, Villejuif, France; Pfizer Oncology, La Jolla, CA; Pfizer Oncology, Shanghai, China; Pfizer Oncology, San Diego, CA; Memorial Sloan Kettering Cancer Center, New York, NY

Background: Axitinib (axi) is approved for 2nd-line treatment of aRCC. In AXIS trial, median progression-free survival (PFS) was significantly longer in axi- vs sorafenib (sor)-treated pts (hazard ratio [HR] 0.67, 95% CI 0.54–0.81, $P<0.0001$). Association between mRNA/miRNA expression and clinical outcomes in a subset of axi- or sor-treated pts from AXIS was assessed. **Methods:** mRNA/miRNA analyses were performed on archival tumor samples. Expression was summarized for responders (complete and partial response) vs non-responders (stable and progressive disease), and for maximum percent tumor change. PFS and overall survival (OS) were analyzed by Kaplan-Meier. **Results:** Pt characteristics were similar between axi (n=34) and sor (n=33) arms. Association with outcomes is shown in the Table. A correlation was observed for CD68 protein and mRNA expression in axi-treated pts (R=0.4774 $P=0.0043$ and R=0.3985 $P=0.0196$, respectively). Both CXCR4 and TLR3 showed differences between treatment arms and association with PFS. TNFSF10 <median, and CD163, CSF1R and miR-221-5p ≥median were associated with shorter OS with axi vs sor ($P<0.05$). Clinical trial information: NCT00678392. **Conclusions:** Immune-related biomarkers were associated with clinical outcomes in axi/sor-treated aRCC pts. Lower CCR7 expression was associated with better response and OS in axi-treated pts. CXCR4 and TLR3 may be predictive of response to axi. Analysis in a larger cohort is warranted.

mRNA/miRNA association with outcomes.

mRNA/miRNA	OR/HR*	95% CI	*P* value
Axi-treated pts			
		Responder vs non-responders	
CCR7 < m	0.11	0.01–1.00	0.026
ITGA4 < m	0.10	0.01–0.98	0.026
VHL < m	0.10	0.01–0.98	0.026
miR-99B-5p ≥ m	NE	NE	0.011
miR-192-3p ≥ m	NE	NE	0.011
		maximum percent tumor change	
CCR7 < m	n/a	n/a	0.004
		PFS	
CXCR4 ≥ m	0.3	0.1–0.8	0.011
TLR3 ≥ m	0.4	0.2–0.9	0.023
miR-133A-3p ≥ m	0.4	0.1–0.9	0.022
miR-143-5p ≥ m	0.4	0.2–1.0	0.037
		OS	
CCR7 < m	3.9	1.4–10.3	0.005
PTPN11 ≥ m	0.4	0.1–0.9	0.02
Sor-treated pts			
		Responder vs non-responders	
ESM1 < m	NE	NE	0.044
NOTCH1 < m	NE	NE	0.044
VHL < m	NE	NE	0.044
GSK3B < m	NE	NE	0.036
TLR3 < m	NE	NE	0.023
		PFS	
TLR3 < m	3.9	1.4–10.7	0.005
		OS	
CCL2 < m	3.1	1.2–8.4	0.019
TLR3 < m	3.0	1.1–8.0	0.022

*Odds ratio (OR) for response; HR for PFS/OS. m=median; NE=not estimable; n/a=not available

615 **Poster Session (Board #G10), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM**

Fecal microbiota transplantation for TKI-induced diarrhea in patients with metastatic renal cell carcinoma.

Ernesto Rossi, Gianluca Ianiro, Brigida Anna Maiorano, Roberto Iacovelli, Loris Lopetuso, Carlo Romano Settanni, Luca Masucci, Gianluca Quaranta, Maurizio Sanguinetti, Emilio Bria, Antonio Gasbarrini, Giampaolo Tortora, Giovanni Cammarota, Giovanni Schinzari; Medical Oncology Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rome, Italy; Gastroenterolgy Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rome, Italy; Gastroenterology Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rome, Italy; Microbiology Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rome, Italy; Medical Oncology Fondazione Policlinico Universitario A. Gemelli IRCCS, Roma, Italy; Medical Oncology Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Roma, Italy; Gastroenterology Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Roma, Italy

Background: Diarrhea is a common adverse event of tyrosine kinase inhibitors (TKI). No standard treatment for TKI-induced diarrhea has been established, although probiotics are commonly used. In several patients TKI dose reduction is necessary. Data showing the interplay between microbiota and TKI-induced diarrhea are reported. The therapeutic modulation of gut microbiota could be useful to ameliorate TKI-related diarrhea. Our study aims to explore the efficacy and safety of fecal microbiota transplantation (FMT), compared with current clinical practice approach, for the treatment of TKI-associated diarrhea in patients with metastatic renal cell carcinoma. **Methods:** Patients on treatment with Pazopanib/Sunitinib as first line therapy for metastatic renal cell carcinoma and TKI-associated diarrhea (^{3} 4 stools per day over baseline) were randomize to receive FMT from healthy donor by colonoscopy (fresh faeces) or probiotics (L. casei DG). The primary endpoint was the resolution of TKI-related diarrhea. Baseline fecal samples were collected from all patients and donors. All patients were followed up 7, 15, 30 and 60 days after the treatment for diarrhea. **Results:** 21 subjects, 10 in FMT arm and 11 in control arm, have been enrolled. At 7 day-follow-up, TKI-related diarrhea disappeared in 10 patients of the FMT group and in 6 patients of the control group (100% vs 54.5%, p = 0.02). At 15-day and 30-day, 9 patients in the FMT group and 0 patients in the control group experienced resolution of diarrhea (90% vs 0%, p = 0.0001). At 60-days 8/10 patients in FMT arm did not have diarrhea. Dose reduction was necessary in 4 patients of the control group. No serious adverse events associated with any of the two treatment protocols were observed. Metagenomic analyses on collected stool samples are ongoing. **Conclusions:** This open-label randomised controlled trial showed the effectiveness and safety of FMT compared with probiotics in curing TKI-related diarrhea in patients with metastatic renal cell carcinoma, avoiding the necessity of dose reduction. Considering the increasing evidence, the modulation of microbiota trough FMT could also affect the efficacy of immunotherapy for metastatic renal cell carcinoma.

616 **Poster Session (Board #G11), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM**

A prospective phase II trial of gemcitabine plus axitinib in patients with sarcomatoid type renal carcinoma.

Inkeun Park, Hyo Jin Lee, Woo Kyun Bae, Shinkyo Yoon, Jae-Lyun Lee; Division of Medical Oncology, Department of Internal Medicine, Gachon University Gil Medical Center, Inchon, Korea, Republic of (South); Chungnam National University Hospital, Daejeon, Korea South; Chonnam National University Medical School, Gwangju, Korea, Republic of (South); Department of Oncology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea, Republic of (South); Asan Medical Center and University of Ulsan College of Medicine, Seoul, Korea, Republic of (South)

Background: Sarcomatoid renal cell carcinoma (SRCC) is a rare but very aggressive type of RCC. The treatment option for SRCC is very limited, and there have been anecdotal reports of very good responders to gemcitabine or vascular endothelial growth factor receptor tyrosine kinaase inhibitors (VEGFR TKI). We conducted multicenter phase 2 trial of gemcitabine plus axitinib (GX) in patients (pts) with recurrent or metastatic SRCC to evaluate its efficacy and safety. **Methods:** Eligibility criteria included histologically confirmed metastatic or recurrent RCC with sarcomatoid component of 25% or more on resected kidney or exclusive sarcomatoid carcinoma on needle biopsy, ECOG PS 0-2, measurable lesion by RECIST v1.1, and adequate cardiac, hepatic, renal and bone marrow function. Pts with uncontrolled hypertension, prior exposure to gemcitabine or VEGFR TKI were exclude. Pts received gemcitabine 1,000 mg/m2 intravenously on days 1 and 8 by 3-week cycle and axitinib 5 mg twice daily. The primary endpoint was objective response rate (ORR) according to RECIST v1.1, and secondary end points were progression-free survival (PFS), overall survival (OS), and toxicity. **Results:** Twenty-five pts were enrolled between Oct 2014 and Aug 2018. Median age was 61 (range 33-80), and 84% was male. ECOG PS were 1 (92%) and 2 (8%), and 52% had prior nephrectomy. Clear cell carcinoma was the most common histology of carcinoma component, and median percentage of sarcomatoid component was 90% (25-100%). Pts belonged to intermediate (28%) and poor (72%) risk group according to IMDC risk stratification. Median 6 cycles of GX were administered, and 56%, 28%, and 12% of pts achieved PR, SD, and PD, respectively, with an ORR of 56% and median duration of response of 2.5 months. With a median follow-up duration of 21.4 mo, median PFS was 4.9 mo (95% CI, 3.5-13.3), and median OS was 8.4 months (95% CI 3.5-13.3 months). Most adverse events were manageable, and no unexpected toxicities were found. One pt died of grade 5 pneumonia. **Conclusions:** GX showed promising efficacy in pts with SRCC. GX might be considered as one of treatment options for pts with SRCC, although efficacy of GX should be confirmed in larger trial.

617 Poster Session (Board #G12), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM

The association of anxiety and depression with mortality risk among patients with clear cell renal cell carcinoma undergoing nephrectomy.

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Background: Anxiety and depression are psychosocial factors which have been demonstrated to have mixed interactions with mortality across various malignancies. While these variables have been associated with poor overall survival for patients with metastatic RCC, the influence on outcomes for localized RCC has been poorly studied. We evaluated the association of anxiety or depression with survival in patients with surgically treated localized clear cell RCC (ccRCC). **Methods:** We performed retrospective review of our institutional nephrectomy registry to identify 1,990 patients who underwent radical or partial nephrectomy for unilateral, sporadic, non-metastatic ccRCC between 1995- 2011. Baseline anxiety and depression were identified using ICD-9 codes. Associations of anxiety or depression with outcomes of interest were evaluated using Cox proportional hazards models. Two propensity score (PS) techniques were used: adjusting for PS quintile and re-weighting by stabilized inverse probability weights. **Results:** A total of 197 (10%) patients had diagnoses of anxiety or depression (57 had anxiety alone, 107 had depression alone, and 33 had both anxiety and depression). Median follow-up among survivors was 10.0 (IQR 7.3-13.6) years, during which time 864 died, including 363 from RCC. Patients with anxiety or depression were younger (mean age 59 vs 62 years, $p < 0.001$) and had more recent operations (75% vs 47% in 2005-2011, $p < 0.001$) compared to those with neither diagnosis. After PS adjustment, all clinical and pathologic features were well balanced between groups. After PS adjustment, there were no significant differences in time to local ipsilateral recurrence, distant metastases, and death from RCC between groups. We did note a trend to poorer overall survival in patients with anxiety or depression (HR 1.29, 95%CI = 0.98-1.69, p = 0.065). **Conclusions:** Our results suggest that neither anxiety nor depression is significantly associated with oncologic outcomes among patients with localized surgically treated ccRCC. The trend toward worse overall survival among patients with anxiety or depression warrants further investigation.

618 Poster Session (Board #G13), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM

Proposal for tripartite re-classification of T1 renal cell carcinoma into cT1a (very low risk), cT1b (low risk), and cT1c (intermediate risk) substages.

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Background: Criteria for staging of T1 renal tumors into T1a (≤4cm) and T1b (4cm< and ≤7cm) have remained unchanged since 1997. Advancements in tumor biology have noted the heterogeneous potential of T1 renal tumors. We hypothesized that a three-tier classification may more rationally risk stratify T1 renal masses than the current T1a/T1b system. **Methods:** Multicenter (UCSD, Fox Chase Cancer Center, Ospadele San Raffaele) retrospective analysis of patients with cT1 renal cell carcinoma treated between 1987 and 2018. Patients were stratified into three groups: cT1a (≤2cm, very low risk), cT1b (2cm< and ≤5cm, low risk), and cT1c (5cm< and ≤7cm, intermediate risk). Primary outcome was recurrence free survival (RFS). Secondary outcome was overall survival (OS). Multivariable Cox Regression analysis (MVA) and Kaplan-Meier analyses (KMA) were utilized. **Results:** 3,324 patients were stratified into proposed T1 groups (T1a=578, T1b=2111, T1c=635; median follow-up 50 months). For cT1a, cT1b and cT1c, KMA revealed 5 year RFS of 96.9%, 91.6%, and 80.6% ($p<0.001$), and 5 year OS of 91.9%, 86.3%, and 76.2% ($p<0.001$). MVA for RFS revealed increasing age (HR=1.02, $p<0.001$), diabetes mellitus (HR=1.36, p=0.04), high tumor grade (HR=2.22, $p<0.001$) and tumor stage (Referent T1a; cT1b HR=2.18 p=0.001, cT1c HR=5.01 $p<0.001$) as independent risk factors. MVA for OS revealed increasing age (HR=1.05, $p<0.001$), diabetes mellitus (HR=1.57, $p<0.001$), high tumor grade (HR=1.34, p=0.002) and tumor stage (Referent T1a; cT1b HR=1.26 p=0.1, cT1c HR=2.050 $p<0.001$) as risk factors. **Conclusions:** Subclassification of cT1 renal cell carcinoma into three clinical stage categories corresponds to distinctive tumor groups whose biological potential varies significantly. Division into three distinct categories may enhance risk stratification, refine preoperative counseling, and augment post-operative follow-up protocols by delineating a very low risk and intermediate risk subset of renal tumors.

Survival Outcomes	5 year	Log Rank
OS		*<0.001*
cT1a (≤2cm)	91.9	
cT1b (2cm< and ≤5cm)	86.3	
cT1c (5cm< and ≤7cm)	76.2	
RFS		*<0.001*
cT1a (≤2cm)	96.9	
cT1b (2cm< and ≤5cm)	91.6	
cT1c (5cm< and ≤7cm)	80.6	

619 Poster Session (Board #G14), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM

Safety and feasibility of nephrectomy after receipt of immune checkpoint inhibitors for renal cell carcinoma.

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Background: With the approval of immune checkpoint inhibitors (ICI) for metastatic renal cell carcinoma (RCC), the role, timing, and safety of surgically excising the primary tumor remain unclear. We sought to evaluate the safety and feasibility of nephrectomy following receipt of ICI for RCC. **Methods:** We reviewed our experience of RCC patients who underwent nephrectomy from 2016-2018 following exposure to nivolumab or combination ipilimumab/nivolumab. Demographics, IMDC risk score, and pathology were collected. Surgical outcomes including operative time (OT), estimated blood loss (EBL), hospital length of stay (LOS), readmission rates, and 30- and 90-day complication rates were analyzed using descriptive statistics. **Results:** 11 nephrectomies (10 radical, 1 partial) were performed in 10 patients after ICI with median postoperative follow-up 98 days. 6 patients received 1-4 cycles of ipilimumab/nivolumab, while 5 received 2-12 infusions of nivolumab preoperatively. One patient with non-metastatic, synchronous bilateral renal masses underwent staged left radical nephrectomy and right partial nephrectomy. 5 surgeries were performed laparoscopically, and 4 patients underwent thrombectomy. IMDC score for metastatic patients was intermediate (7/9) or poor (2/9). One patient exhibited complete response (pT0) to ICI, and 3/4 patients who underwent metastasectomy for hepatic, pulmonary, or adrenal lesions exhibited no malignancy in any of the metastases resected. No patients experienced any major intraoperative complications, and all surgical margins were negative. Median OT, EBL, and LOS were 180 minutes, 100 mL, and 4 days, respectively. One patient died of progressive disease $>$ 3 months after surgery; one patient required thoracentesis and another required paracentesis of a sterile fluid collection in the hepatic resection bed. No complications were noted in the remaining 7 patients, none of whom required readmission. **Conclusions:** Nephrectomy following ICI for RCC is safe and technically feasible with favorable surgical outcomes and pathologic response. As multimodal management in the era of ICI continues to evolve, use of neoadjuvant ICI for selected patients may warrant attention.

620 Poster Session (Board #G15), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM

Fumarate hydratase expression in localized, radically-resected clear cell renal cell carcinoma and its association with clinical outcomes.

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Background: Prognostic stratification of localized clear cell renal cell carcinoma (lccRCC) mainly relies on clinical characteristics and TNM staging system, while biological biomarkers are currently lacking. We previously showed that reduced expression of the tricarboxylic acid cycle enzyme fumarate hydratase (FH) was associated with better clinical outcomes in patients (pts) with metastatic ccRCC. In the present study we aimed at assessing the association between intratumor FH expression and clinical outcomes in pts with radically-resected lccRCC. **Methods:** Pts with radically-resected lccRCC and available formalin-fixed, paraffin-embedded (FFPE) primary (renal) tumor tissue were included. FH protein expression was assessed by means of immunohistochemistry (IHC) and defined as normal (comparably to non-neoplastic tubular cells) or low (lower than in non-neoplastic tubular cells). **Results:** Out of 50 pts included, we found a normal FH expression in 20 cases (40%) and a low FH expression in 30 cases (60%). Median age was 57 years (interquartile range 49-68) and 48 pts (96%) had pN0 disease, while 2 pts (4%) had pN1 disease. Low FH expression was associated with pT (*P*= .003) but not with sex, age, Fuhrman grade or pN. After a median follow-up of 76.9 months, low FH expression was associated with a lower relapse rate (13% vs 50%; odds ratio for relapse 0.16; 95% confidence interval [CI] 0.04-0.62; *P*= .005), longer relapse-free survival (RFS) (5-years RFS rate 90% vs 50%; HR 0.20; 95% CI 0.06-0.63; *P*= .006) and a trend toward a better overall survival (OS) (5-years OS rate 100% vs 77.3%; HR 0.14; 95% CI 0.02-1.23; *P*= .07) when compared with normal FH expression. In the multivariable model including other characteristics associated with RFS, low FH expression confirmed an independent association with RFS (adjusted HR 0.25; 95% CI 0.06-0.91; *P*= .03). **Conclusions:** In our study, low intratumor FH, as detected by IHC, was associated with lower relapse rate, better RFS and a trend toward a better OS in patients with lccRCC when compared with normal FH levels. The role of FH expression as a prognostic biomarker in this setting warrants further investigation.

621 Poster Session (Board #G16), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM

The role of radiomics in the preoperative diagnosis of renal cell carcinoma with sarcomatoid dedifferentiation (sRCC).

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Background: sRCC is an aggressive renal malignancy, with poor survival and limited response to therapy. Preoperative identification of sRCC would be helpful for counselling patients, and clinical trial enrollment. This study aims at assessing the potential of radiomics to discriminate clear cell sRCC from non-sarcomatoid clear cell RCC (nsRCC). **Methods:** The study included 49 sRCC and 41 nsRCC patients treated with surgery between 2007-2016, who had contrast-enhanced CT available. An experienced radiologist delineated the entire tumor using 3D Slicer (http://www.slicer.org). The extracted 3D region of interest was imported in our in-house radiomic pipeline. A total of 310 features (10 histogram-based and 300 second-order features) were calculated. Second-order radiomic features were calculated using the Grey Level Cooccurrence Matrix (GLCM) and 20 Haralick features were obtained from the GLCM. To account for directionality, the mean, variance and range of the features across different directions were calculated. Finally, different number of gray levels were also considered in the analysis (N = 8, 16, 32, 64, 256). Core features were obtained using a feature selection based on Least Absolute Shrinkage and Selection Operator (LASSO). Selected features were used to build a classification model for prediction of sRCC versus nsRCC (XGboost). To evaluate the robustness of the estimates, Leave One Out Cross-Validation (LOOCV) was conducted on the patient set. **Results:** Overall, median tumor size was 10.0 cm and most patients had pT3a (68%). There was no significant difference of age, gender, race, tumor size and stages between sRCC and nsRCC cohorts. The prediction of sRCC using LOOCV was significant with p-value < 0.0001. Area under the curve, sensitivity, and specificity for identification of sRCC were 96.8%, 92.6% and 93.8% respectively. **Conclusions:** This study demonstrates that CT radiomic features can accurately discriminate between sRCC and nsRCC. The proposed tool has the potential to advance clinical management strategies. In addition to being noninvasive, this methodology can be applied to scans obtained during routine clinical care. Further external validation is warranted.

622 **Poster Session (Board #G17), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM**

Duration of treatment (DOT) with targeted therapies (TT) or immunotherapy (IO) in PBRM1 mutated metastatic renal cell carcinoma (mRCC).

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Background: Current evidence indicates improved outcome with IO in mRCC patients (pts) with PBRM1 loss of function mutations (Miao et al., Nature, 2018). We seek to demonstrate an association between PBRM1 mutation and treatment duration with IO and TT in a retrospective cohort. **Methods:** Consecutive patients with mRCC who had genomic profiling in the course of routine clinical care were identified from an institutional database. GP assessments included testing either tissue or blood with 1 of the 3 CLIA certified commercial panels (Foundation Medicine, Cambridge, MA; Ashion Analytics, Phoenix, AZ; Guardant Health, Redwood City, CA). Information regarding systemic treatment was collected. Median DOT with first targeted therapy and first immunotherapy received was calculated for each patient. DOT was compared across treatment groups in PBRM1+ and PBRM1- patients. Only PBRM1 mutations with functional significance documented in COSMIC were considered. **Results:** Among 104 pts (72:32 M:F) with mRCC, 82 pts received TT, 35 pts received IO, and 45 pts received both. GP was performed in blood and tissue in 84 and 63 pts, respective, and 25 pts (24%) with PBRM1 mutations were identified. Among PBRM1+ pts, median DOT was 8.8 months (95% CI, 7.6-9.6) mos and 2.3 mos (95% CI, 1.7 – 2.8) mos with TT and IO, respectively (p=0.049). Among PBRM1- pts, median DOT was 5.5 mos and 2.8 mos with TT and IO, respectively (p=0.544). There were 11 PBRM1+ pts and 34 PBRM- pts who received both TT and IO. The ratio of DOT on IO to DOT on TT ($DOT_{IO/TT}$) was higher in PBRM1- pts than PBRM1+ pts (0.76 versus 0.37 respectively, p=0.014). **Conclusions:** We failed to replicate the results from Miao *et al,* suggesting clinical benefit with IO in PBRM1 mutated patients. PBRM1 mutation did appear to predict benefit with TT versus IO. Although limited by sample size, the contrasting results of the current study with literature highlight the importance of clinical validation in a large and prospective setting.

623 Poster Session (Board #G18), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM

Prognostic value of gain of chromosome 5q in localized renal cell carcinoma.

Cedric Michel Lebacle, Aydin Pooli, Nagesh Rao, Erika Louise Wood, Nils Kroeger, Sandy Liu, Izak Faiena, Karim Chamie, Arie S. Belldegrun, Brian Shuch, Alexandra Drakaki, Allan J. Pantuck; Institute of Urologic Oncology (IUO), Department of Urology, David Geffen School of Medicine at UCLA, Los Angeles, CA, USA Service d'urologie CHU Bicêtre, APHP, Université Paris-Sud Paris Saclay, Le Kremlin Bicetre, France; Institute of Urologic Oncology (IUO), Department of Urology, David Geffen School of Medicine at UCLA, Los Angeles, CA; Department of Pathology and Lab Medicine, David Geffen UCLA School of Medicine, Los Angeles, CA; Department of Urology, David Geffen School of Medicine at UCLA, Los Angeles, CA; Department of Urology, University Medicine Greifswald, Greifswald, Germany; Department of Hematology and Oncology, David Geffen School of Medicine at University of California, Los Angeles, CA; University of California Los Angeles, Los Angeles, CA

Background: While gain of chromosome 5q is a frequently seen cytogenetic abnormality noted to occur in patients with renal cell carcinoma (RCC), little is known about its prognostic significance. We investigated the association of gain of 5q with disease-free survival (DFS) in patients with localized (non-metastatic T1-2) RCC. **Methods:** All patients from UCLA with primary tumor stage T1-2 RCC who had tumor cytogenetic analysis on tumor specimen were included. Alterations in chromosome 5q was specifically reviewed in this study. Logistic regression analyses were used to assess association of gain of 5q with final histopathology, ISUP grading, and T-stage. Cox proportional hazard modeling and Kaplan-Meier analyses were used to assess the impact of gain of 5q on DFS. Recurrence was defined as any local recurrence or development of new metastasis. **Results:** A total of 676 patients were included in this study. Gain of 5q occurred in 108 (16%) patients and was more commonly seen in clear cell versus non-clear cell tumors (19% vs. 9%, p = .002). Gain of 5q was associated with low grade ISUP (1 or 2) of clear-cell RCC (p = 0.011). On survival analysis, there was a 67% decreased risk of RCC recurrence for patients with gain of 5q (HR = 0.33, p = 0.018). The 5- and 10-year risk of recurrence was 2% vs. 16% and 14% vs. 28% for patients with and without gain of 5q, respectively (p = 0.013). In multivariable Cox analysis, the gain of 5q was an independent prognostic factor (p = .026 with ISUP grade and p = .025 with T-stage). These findings were confirmed among clear-cell RCC subgroup. **Conclusions:** Gain of chromosome 5q is an independent prognostic factor associated with decreased risk of recurrence in patients with localized T1-2 renal cell carcinoma. Identifying patients with a gain of 5q will improve the stratification of the risk of recurrence, could allow to adapt the follow-up protocols and avoid adjuvant treatment.

624 Poster Session (Board #G19), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM

Nivolumab in second or third line setting for the treatment of metastatic renal cell carcinoma (mRCC): The real-world experience from Guy's Hospital.

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Background: Nivolumab (Nivo) has been approved by the FDA for patients (pts) with mRCC who have received prior VEGF tyrosine kinase inhibition based on the Checkmate 025 study. However following various new anti-angiogenic therapies licensed over the past decade, optimal sequence of treatments in mRCC remains unknown. **Methods:** This is a retrospective review of mRCC pts who received nivo at Guy's Hospital. Pts were divided based on treatment line setting. Clinical characteristics, response rate (RR), progression free survival (PFS), duration on treatment and safety are reported. **Results:** Between March 2016 and April 2018, 50 pts with mRCC received nivo, 25 as second line (2L) and 25 as third line treatment or beyond (3L+). In 2L setting, median age was 62 years and 68% were male. 76% had a nephrectomy, with a majority of clear cell (cc) histology (92%). 96% of pts had visceral metastases. 88% received pazopanib in the first line setting (1L). Median age for pts in 3L+ was 60 years and 88% were male. 60% had a nephrectomy and 80% had cc histology. 96% had visceral metastases. Pazopanib was given in 72% in 1L. RR was 28% and 16% in 2L and 3L+ respectively. Median duration of treatment was 4.3 months in 2L and 2.2 months in 3L+, with 11 patients (22%) still on treatment. Median follow-up time was 12.4 months in 2L and 9 months in 3L+. Median PFS was 4.8 months and 3.7 months respectively in 2L and 3L+ groups. Median OS was not reached in either group. Adverse events leading to treatment discontinuation occurred in 7 pts (14%). 5 pts experienced grade 3/4 toxicities (colitis, pneumonitis, hepatitis, arthritis and nephritis), with 4 pts in 3L+. Overall 22 pts received subsequent treatments: 8/25 (32%) had cabozantinib (cabo) and 4/25 (16%) were treated with axitinib following nivo given in 2L. For pts who received nivo in the 3L+ setting 7/25 (28%) received cabo and 2/25 (8%) had axitinib as subsequent therapy. **Conclusions:** Our real world data supports the efficacy and safety of nivo following VEGF inhibition for pts with mRCC. Nivo was associated with a trend towards superior clinical responses in the 2L setting. For the entire cohort no new safety signals were reported.

625 Poster Session (Board #G20), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM

Radiomic correlates of molecular and clinicopathological characteristics in clear cell renal cell carcinoma.

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Background: Clear cell renal cell carcinoma (ccRCC) is a highly vascularized tumor and has a heterogeneous molecular profile, but the correlation between its tumor biology and radiomic features have only recently been investigated. As 70% of ccRCCs are detected incidentally at imaging, and tumor phenotypes are only available after surgery, a non-invasive biomarker to predict ccRCC phenotypes and aggressiveness on imaging may be clinically valuable, as low grade lesions may undergo active surveillance. **Methods:** With IRB approval and HIPAA compliance, our study cohort comprised 92 consecutive patients with 102 ccRCCs (mean age, 62 years (SD $\pm$ 14.2) with histopathology and molecular endpoints imaged preoperatively on CT with a four-phase renal protocol [unenhanced (U), corticomedullary (C), nephrographic (N), excretory (E)]. Radiomic data was obtained by contouring the entire ccRCC in each phase to obtain a 3D tumor volume of interest (VOI). The mean enhancement in each phase the and wash-in and wash-out of enhancement was calculated for each ccRCC. Molecular data was obtained through immunohistochemistry of resected ccRCCs to assess carbonic anhydrase-IX (CAIX), microvessel density (MVD), phosphatase and tension homolog (PTEN), and tumor grade (TG). Categorical variables were analyzed with logistic regression and odds ratio (OR) was reported. Continuous variables were analyzed with linear regression and Pearson correlation coefficient (r^2) was reported. *P*-values $<$ .05 were considered significant. **Results:** Significant radiomic associations included TG and 3D tumor enhancement in the C (OR = 4.72, p = .030), N (OR = 17.71, p $<$ .0001), and E phases (OR = 17.10, p $<$ .0001), and wash-in from U to C (OR = 8.27, p = .004). MVD had a significant positive association with 3D tumor enhancement in the C phase (r^2= 0.410, p $<$ .0001), wash-in from U to C (r^2= 0.435, p $<$ .0001) and wash-out from the C to N (r^2= 0.435, p = .001). There were no significant radiomic correlates with CAIX or PTEN expression. **Conclusions:** A 3D ccRCC VOI on multiphasic CT had significant correlations with TG and MVD, independent of clinical features, potentially becoming a predictive imaging biomarker of ccRCC aggressiveness and clinical outcome.

626 Poster Session (Board #G21), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM

Prognostic value of loss of chromosome 10q in patients with localized renal cell carcinoma.

Cedric Michel Lebacle, Aydin Pooli, Nagesh Rao, Erika Louise Wood, Nils Kroeger, Sandy Liu, Izak Faiena, Karim Chamie, Arie S. Belldegrun, Brian Shuch, Alexandra Drakaki, Allan J. Pantuck; Institute of Urologic Oncology (IUO), Department of Urology, David Geffen School of Medicine at UCLA, Los Angeles, CA, USA Service d'urologie CHU Bicêtre, APHP, Université Paris-Sud Paris Saclay, Le Kremlin Bicetre, France; Institute of Urologic Oncology (IUO), Department of Urology, David Geffen School of Medicine at UCLA, Los Angeles, CA; Department of Pathology and Lab Medicine, David Geffen UCLA School of Medicine, Los Angeles, CA; Department of Urology, David Geffen School of Medicine at UCLA, Los Angeles, CA; Department of Urology, University Medicine Greifswald, Greifswald, Germany; Department of Hematology and Oncology, David Geffen School of Medicine at University of California, Los Angeles, CA; University of California Los Angeles, Los Angeles, CA

Background: Several tumor-suppressor genes have been mapped to chromosome 10q, including PTEN. While loss of 10q is a frequently seen cytogenetic abnormality noted to occur in patients with renal cell carcinoma (RCC), little is known about its prognostic significance. We investigated the association of loss of 10q with pathological features and disease-free survival (DFS) in patients with localized RCC. **Methods:** All patients from UCLA with primary localized RCC who had tumor cytogenetic analysis were included. Alterations in chromosome 10q was specifically reviewed for this study. Logistic regression analyses were used to assess association of loss of 10q with ISUP grading, and T-stage. Cox proportional hazard modeling and Kaplan-Meier analyses were used to assess the impact of loss of 10q on DFS and OS. Recurrence was defined as any local recurrence or development of new metastasis after surgery. **Results:** A total of 886 patients were included in this study. Loss of 10q occurred in 68 (7.7%) patients and was more commonly seen in chromophobe subtype (24% vs. 6% in non-chromophobe RCC, $p < .0001$). Loss of 10q was associated with greater tumor size (mean 6.3 vs 5.1 cm, OR = 1.085 [1.024-1.150], p = .008), T3-stage (37% vs 23%, OR = 1.99 [1.17-3.39], p = .011), and ISUP 3-4 (61% vs 37%, OR = 2.64 [1.58-4.40], $p < .0001$). On survival analysis, after a mean follow-up of 55 months, these patients had a shorter time to recurrence (Log-rank p = .026) and a worse DFS (HR = 2.15 [1.32-3.50], p = .002) than those without loss of 10q. These findings were confirmed on clear-cell RCC subgroup with also a worse OS (HR = 2.00 [1.09-3.67], p = .026) with an estimated 34% risk of death at 5 years for patients with loss of 10q. **Conclusions:** Loss of chromosome 10q is a prognostic factor associated with larger tumor size, higher grade and T-stage, and worse survival in patients with localized RCC. Identifying patients with loss of 10q can provide additional prognostic information to clinicopathologic variables.

627 General Session, Sat, 7:55 AM-9:30 AM and Poster Session (Board #D1), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM

The UCLA Histo-Genetic Risk Classification (U-HGRC) to predict outcomes of localized clear cell renal cell carcinoma.

Cedric Michel Lebacle, Aydin Pooli, Nagesh Rao, Erika Louise Wood, Nils Kroeger, Hyun J. Kim, Izak Faiena, Sandy Liu, Karim Chamie, Arie S. Belldegrun, Brian Shuch, Alexandra Drakaki, Allan J. Pantuck; Institute of Urologic Oncology (IUO), Department of Urology, David Geffen School of Medicine at UCLA, Los Angeles, CA, USA Service d'urologie CHU Bicêtre, APHP, Université Paris-Sud Paris Saclay, Le Kremlin Bicetre, France; Institute of Urologic Oncology (IUO), Department of Urology, David Geffen School of Medicine at UCLA, Los Angeles, CA; Department of Pathology and Lab Medicine, David Geffen UCLA School of Medicine, Los Angeles, CA; Department of Urology, David Geffen School of Medicine at UCLA, Los Angeles, CA; Department of Urology, University Medicine Greifswald, Greifswald, Germany; Department of Biostatistics, Fielding School of Public Health at UCLA, Department of Radiological Science, David Geffen School of Medicine at University of California, Los Angeles, CA; Department of Hematology and Oncology, David Geffen School of Medicine at University of California, Los Angeles, CA; University of California Los Angeles, Los Angeles, CA

Background: Thirty percent of patients with localized clear cell renal cell carcinoma (ccRCC) will ultimately develop recurrence (local or metastatic) after nephrectomy. Current risk stratification systems still misclassify patients. We have developed a novel classification integrating cytogenetic findings to better stratify the risk of recurrence and overall survival (OS) after surgery for localized ccRCC. **Methods:** A total of 646 patients from UCLA with ccRCC and tumor cytogenetic analysis, were included in this study. After a selection of histologic parameters using logistic regression and cytogenetic parameters using principal component analysis a CHAID decision tree and Kaplan Meier analysis were used to build the UCLA Histo-Genetic Risk Classification (U-HGRC). Survival analyses of the model were validated on two random samples of 323 patients. Recurrence was defined as any local recurrence or development of new metastasis after surgery. **Results:** The T-stage, tumor size, presence of sarcomatoid features, gain of chromosome 5q, loss 10q, or loss X/Y were used to stratify the risk of recurrence of ccRCC into three U-HGRC groups of low (1), intermediate (2) or high-risk (3). After a mean follow-up of 55 months, risk of recurrence (HR = 2.44, p = .001 for U-HGRC 2; HR = 9.90, $p < .0001$ for U-HGRC 3), disease-free survival (DFS) (Log-rank $p < .0001$), risk of death (HR = 1.72, p = .033 for U-HGRC 2; HR = 4.74, $p < .0001$ for U-HGRC 3) and OS (Log-rank $p < .0001$) were significantly different between groups. These findings were validated on two random samples. For high-risk group, median DFS and OS were 2.7 and 6.3 years, respectively. The 5-year risks of recurrence for U-HGRC group 1, 2 and 3 were 9%, 25% and 62%, respectively. The AUC of the model was significantly improved comparing to the current UISS system (0.72 for U-HGRC vs 0.65 for UISS, p = .008) with an accuracy of 82.8% for the U-HGRC high-risk group. **Conclusions:** The U-HGRC, which integrates genomic alterations with clinical and pathologic features, allowed a better stratification of recurrence risk and overall survival that could help to select appropriate patients for surveillance and adjuvant therapy protocols.

628 Poster Session (Board #H1), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM

Are patients ready to participate in diet intervention trials in oncology? Experience from renal cell carcinoma (RCC) patients.

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Background: Diet intervention in oncology is currently under investigation. Nevertheless, some cancer patients are increasingly using various diet interventions with the hope to optimize the anti-tumor response or to control the side effects of oncological treatment. Thus, well conducted prospective trials are required. In order to design such trials, we conducted a prospective study in order to estimate(a) the number of patients already using diet interventions on their own and (b) the percentage of patients who would agree to follow a restrictive diet in combination to antitumoral treatment within a prospective trial, if offered by their oncologist. **Methods:** Metastatic RCC patients seen at a single institution as outpatient clinic between April and May 2018, were offered to take part in an anonymous feasibility questionnaire. Questions included current treatment status for RCC, gender, height, and weight and explored (a) self diet restriction practices and (b) willingness to take part in trial(s) that would evaluate various diet interventions: fasting, ketogenic, vegetarian or vegan diets (each of them being explained). The proposed diet intervention was supposed to be for a minimum of 3 months. **Results:** Overall, 119 patients filled out the questionnaire. Median age was 61,5 years, 79(66.3%) were under systemic treatment. At time of data collection, 7.5% patients reported ketogenic diet practices, 0.9% fasting, none vegan or vegetarian diet. Regarding willingness to take part in "diet therapeutic trials", 42.0% of patients claimed to agree to participate in a ketogenic diet trial, 29.4% of patients would agree to take part in a trial exploring fasting, 28.5% a vegetarian diet trial, and 14.2% of patients a vegan diet trial. No link between being under treatment and willingness to participate in trial was observed (p = 0.365). **Conclusions:** For the first time, we report feasibility of diet intervention within an homogenous population of patients with RCC. Almost half of patients are really keen in participating, with more interest for ketogenic diet and fasting. Such study raises the question of the feasibility of such trials, and obviously would make randomized trials very challenging.

629 Poster Session (Board #H2), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM

Improving the definition of high-risk patients for tumor recurrence from clear cell renal cell carcinoma: The U-CISS classification.

Cedric Michel Lebacle, Nils Kroeger, Aydin Pooli, Sandy Liu, Karim Chamie, Arie S. Belldegrun, Brian Shuch, Alexandra Drakaki, Allan J. Pantuck; Institute of Urologic Oncology (IUO), Department of Urology, David Geffen School of Medicine at UCLA, Los Angeles, CA, USA Service d'urologie CHU Bicêtre, APHP, Université Paris-Sud Paris Saclay, Le Kremlin Bicetre, France; Department of Urology, University Medicine Greifswald, Greifswald, Germany; Institute of Urologic Oncology (IUO), Department of Urology, David Geffen School of Medicine at UCLA, Los Angeles, CA; Department of Hematology and Oncology, David Geffen School of Medicine at University of California, Los Angeles, CA; University of California Los Angeles, Los Angeles, CA

Background: Thirty percent of patients with localized clear cell renal cell carcinoma (ccRCC) will ultimately develop recurrence (local or metastatic) after nephrectomy. Current risk stratification systems still misclassify patients. A better stratification is needed to select high-risk patients who may benefit from adjuvant therapy. We sought to improve the existing UISS by the addition of genetic information in a new UCLA cytogenetic integrated staging system (U-CISS). **Methods:** A total of 240 patients from UCLA with localized ccRCC and cytogenetic analysis on tumor specimen were included in the study. In a continuation of our previous research, cytogenetic (combined loss 3p-14q) and a pathological high-risk feature, microvascular invasion (MVI) were implemented in the UISS. Association with recurrence free survival (RFS) was analyzed in a uni- and multivariable fashion; prognostic accuracy was tested with the c-index. All tumors that had either MVI, combined loss 3p/14q or both in the UISS low-risk group were placed into the U-CISS intermediate group. Tumors with one or both risk factors in the UISS intermediate group were placed into the new U-CISS high-risk group. **Results:** Fifty patients developed tumor recurrence. On multivariate analysis, combined loss 3p-14q, and MVI were independent prognostic factors. The U-CISS placed significantly better prognosticated RFS in the high-risk group (7/50 (14%) with UISS vs. 23/50 (46%) with U-CISS) and thus, was more accurate in prognosticating RFS. The c-index for recurrence prognostication was improved in the U-CISS (0.70 vs. 0.65 for the UISS). Furthermore, the U-CISS was a better prognostication tool when the intermediate and high-risk group were combined (prognostication of 74% with U-CISS vs. 68% UISS). **Conclusions:** The use of U-CISS, which integrates genomic alterations with clinical and pathologic features, allowed a re-allocation of patients to create a better stratification of recurrence risk. This new definition of high-risk of recurrence could significantly improve selection of patients who are in greatest need of closer surveillance and/or adjuvant treatment. *C.L. and N.K. contributed equally to first authorship.*

630 Poster Session (Board #H3), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM

Combination anti-angiogenic tyrosine kinase inhibition and anti-PD1 immunotherapy in metastatic renal cell carcinoma: A retrospective analysis of safety, tolerance, and clinical outcomes.

Andrew L. Laccetti, Minas P. Economides, Aradhana M. Venkatesan, Jianjun Gao, Eric Jonasch, Paul Gettys Corn, Amado J. Zurita, Nizar M. Tannir, Pavlos Msaouel, Amishi Yogesh Shah, Matthew T Campbell; MD Anderson Cancer Center, Houston, TX; Department of Infectious Diseases, The University of Texas MD Anderson Cancer Center, Houston, TX; UT MD Anderson Cancer Center, Houston, TX; The University of Texas MD Anderson Cancer Center, Houston, TX; University of Texas MD Anderson Cancer Center, Houston, TX; Department of Genitourinary Medical Oncology, Division of Cancer Medicine, The University of Texas MD Anderson Cancer Center, Houston, TX

Background: Emerging phase III data support combination antiangiogenic tyrosine kinase inhibitors (TKIs) and immunotherapy (IO) as front line treatment for metastatic renal cell carcinoma (mRCC). Little is known about off-protocol experience and later line treatment with this therapeutic approach including tolerance, response and survival. **Methods:** We conducted a retrospective analysis of mRCC patients (pts) who received combination TKI-IO between 11/2015 and 05/2018 at MD Anderson Cancer Center. Chart review detailed baseline characteristics, TKI-IO treatment, toxicity and survival. An independent radiologist, blinded to pts history and clinical data, assessed radiographic response using RECIST v1.1. **Results:** 36 mRCC pts were identified for study inclusion: median (med) age 63.5 years, 72% clear cell histology, 53% intermediate risk (19% good, 28% poor) by IMDC, med metastatic sites 2, med prior therapies 2, previous TKI 94% and previous IO 47%. Combinations included nivolumab (nivo)-cabozantinib (15), nivo-low dose pazopanib(ldP) (13), nivo-axitinib (5), nivo-lenvatinib (2) and pembrolizumab-axitinib (1). Median time on TKI-IO was 5.6 months (m) (95% CI: 5.2 - 7.7). 56% of pts initiated TKI prior to IO addition at progression and 36% of pts initiated IO prior to TKI addition. ORR was 35% (29% PR and 6% CR); disease control rate was 78% (43% stable disease). With med follow-up of 8.0 m (95% CI: 6.4 – 9.4), med PFS was 7.7 m (95%CI: 5.8 - 9.5), med OS was not reached. Med PFS for pts receiving nivo-ldP was not reached. TKI-IO therapy was well tolerated with only 1 pt demonstrating grade 3 or 4 immune related toxicity (nephritis). 92% of pts experienced any grade of adverse events (ADE) with ADE of interest as follows: diarrhea (25%), hypothyroidism (17%), and pneumonitis (8%). **Conclusions:** To our knowledge, this is the first case series of off-label combinations of TKI-IO for mRCC. TKI-IO, particularly nivo-ldP, is safe, well tolerated and efficacious. Although further prospective research is essential, TKI-IO could be considered for select mRCC patients, particularly in the setting of TKI or IO refractory disease.

631 Poster Session (Board #H4), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM

Identifying predictive biomarkers for metastatic progression in stage I and II clear cell renal cell carcinoma.

Neal J Murphy, Andrew Shih, Zachary Kozel, Paras Shah, Oksana Yaskiv, Houman Khalili, Anthony Liew, Louis R Kavoussi, Simon Hall, Manish Arvind Vira, Annette Lee, Xinhua Zhu; Donald and Barbara Zucker School of Medicine at Hofstra/ Northwell, Manhasset, NY; Feinstein Institute for Medical Research, Manhasset, NY; The Smith Institute for Urology, New Hyde Park, NY; Mayo Clinic, Rochester, MN; Northwell Health Department of Pathology, New Hyde Park, NY; Northwell Health Cancer Institute, Lake Success, NY

Background: For most clear cell renal cell carcinoma (ccRCC) patients with early stage disease, surgical resection offers definitive cure. However, for the small percentage of tumors that metastasize, analyzing gene expression profiles from the primary site at the time of nephrectomy can serve as a model to understand the molecular aberrations behind a metastatic phenotype. Differences in gene expression profiles between patients with Stage I and II ccRCC who experience metastasis versus patients who maintain cure after surgery may help elucidate significant molecular targets and stratify patients at higher risk for metastasis. **Methods:** Nineteen Stage I and twenty Stage II ccRCC tumors preserved in FFPE blocks after nephrectomy were included in this study. Patients were matched for age, gender, tumor size and grade. In both stages, approximately half the patients that experienced metastasis within 5 years of surgery were part of the experimental group, whereas the control group had $>$ 5 years of follow-up without evidence of disease. Extracted RNA for Stage I patients was sequenced using Illumina TruSeq RNA Access Library. Gene counts were assessed by ht-seq counts and differential expression using DESeq2. Significant genes found were validated in the Stage II group using RT-qPCR. **Results:** In the Stage I experimental group, statistically significant upregulation of several genes associated with unfavorable prognosis in RCC were found: COL1A1, NUMBL, and STEAP3. Random forest classification accurately separated Stage I control versus experimental patients based on expression of COL1A1. Affected genes were consistent with molecular changes seen in TCGA analysis. In the Stage II group, a double-blinded analysis correctly identified the clinical outcome for the majority of the patients using qPCR expression of COL1A1, NUMBL, and STEAP3. **Conclusions:** Differences in gene expression profiles harbored in the primary site of early stage ccRCC may be employed to predict patients at high risk for developing metastasis. Validating these findings in a larger study carries the potential to better understand mechanisms of metastasis and identify an at risk cohort of patients with early stage disease.

632 **Poster Session (Board #H5), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM**

The role of architectural patterns and cytologic features in the prognosis of clear cell renal cell carcinoma.

Qi Cai, Alana Christie, Qinbo Zhou, Ellen Araj, Jeffrey A Cadeddu, Vitaly Margulis, Nirmish Singla, Satwik Rajaram, Ivan Pedrosa, Dinesh Rakheja, Renee McKay, James Brugarolas, Payal Kapur; UT Southwestern Medical Center, Dallas, TX; University of Texas Southwestern Medical Center, Dallas, TX; The University of Texas Southwestern Medical Center, Dallas, TX

Background: Clear cell renal cell carcinoma (ccRCC) exhibits a spectrum of clinical behavior and intratumoral heterogeneity histologically. Pathologic grading for ccRCC is primarily based on nucleolar size. Sarcomatoid and rhabdoid changes are known to be associated with aggressive behavior, the significance of the histopathologic heterogeneity occurring in ccRCC remains largely unknown. We evaluated the prognostic role of architectural patterns and cytologic features in ccRCC. **Methods:** We identified sequential ccRCC cases at our institution between 2006 and 2015 for which follow-up information was available beyond 1.5 years, excepting those who died sooner. Architectural patterns and cytologic features were predefined and quantitated in nephrectomy specimen slides, which were reviewed by an experienced GU pathologist. Nine novel architectural patterns and ten cytologic features were correlated with disease-free survival (DFS) and overall survival (OS). Kaplan-Meier curves were generated to visualize survival distributions. **Results:** 549 cases met selection criteria and were comprehensively reviewed including 16 grade 1 (2.9%), 278 grade 2 (50.6%), 201 grade 3 (36.6%) and 54 grade 4 (9.8%). Pathologic tumor stage distribution included 63.9% pT1 (n = 351), 6.0% pT2 (n = 33), 27.5% pT3 (n = 151), and 2.6% pT4 (n = 14). Microcystic, tubular, bleeding follicles, and small compact nest patterns (n = 309), were associated with better DFS and OS. In contrast, large nests, thick trabecular, solid sheet, alveolar or papillary/pseudopapillary patterns (n = 240) were associated with worse DFS and OS ($p < 0.0001$). In addition to multinucleated giant cells, and sarcomatoid and rhabdoid changes, cytologic features including large intracytoplasmic eosinophilic inclusions, voluminous cytoplasm, cytoplasmic spindling, a giant nucleus with perinuclear halo, and a wrinkled nucleus with perinuclear halo were associated with worse DFS and OS ($p < 0.0004$). **Conclusions:** Architectural patterns and cytologic features observed in ccRCC predict tumor behavior and are associated with clinical prognosis. Evaluation of histopathologic heterogeneity may shed light on tumor biology and complement prognostic models.

633 Poster Session (Board #H6), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM

Comprehensive molecular and genomic characterization of pancreatic tropism in metastatic renal cell carcinoma.

Nirmish Singla, Jacob Choi, Oreoluwa Onabolu, Layton Woolford, Christina Stevens, Vanina Tcheuyap, Tiffani McKenzie, Zhiqun Xie, Tao Wang, Renee McKay, Alana Christie, Payal Kapur, Brian I. Rini, James Brugarolas; University of Texas Southwestern Medical Center, Dallas, TX; Cleveland Clinic Taussig Cancer Institute, Cleveland, OH

Background: Patients with metastatic renal cell carcinoma (mRCC) involving the pancreas have been shown to exhibit a relatively indolent course, yet the biologic explanation is unclear. We sought to characterize the genomic landscape of patients with mRCC harboring pancreatic metastases to identify molecular drivers of pancreatic tropism. **Methods:** mRCC patients harboring pancreatic metastases from UTSW and Cleveland Clinic were identified. Clinicopathologic data and oncologic outcomes were analyzed. Samples were obtained from primary tumors, metastatic sites (including pancreatic or other distant metastases), and matched normal tissue. Whole exome (WES) and RNA sequencing of tumors was conducted. Patient-derived xenograft (PDX) models were generated from a subset of patients, and the engrafted tumors were analyzed. **Results:** 31 mRCC patients with pancreatic metastases were included with 54 tumor samples derived from the primary tumor or thrombus (24), pancreatic metastasis (21), or other metastatic sites (9). Median follow-up was 101 months. Clinicopathologic characteristics were similar between the two institutional cohorts, and all but one patient were favorable or intermediate IMDC risk. All patients had clear cell histology. 8 patients (26%) were metastatic at diagnosis, and median time to metastasis in the remaining patients was 74 months (IQR 32-120). Overall (OS) and cancer-specific (CSS) survival did not vary by IMDC risk group. Morphologically, tumors largely displayed low-grade acinar patterns. WES with matched normal tissue and RNAseq were completed with adequate quality for 48 and 30 samples, respectively. 14 PDX lines were generated, of which 5 (36%) engrafted stably ($\geq$2 passages). WES from 2 tumorgraft specimens revealed preservation of specific mutations in the corresponding human samples. **Conclusions:** mRCC patients with pancreatic metastases exhibit remarkably favorable survival outcomes. The relatively indolent biology of these tumors is reflected histologically and genomically and can be recapitulated in PDX models. Understanding tumor heterogeneity may help refine prognostic models for mRCC and hold implications for improved personalization of therapy.

634 Poster Session (Board #H7), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM

Adiponectin-AdipoR1 axis in renal cell carcinoma plays a pivotal role in tumor progression and drug resistance.

Guangxi Sun; West China Hospital, Chengdu, China

Background: It is well established that renal cell carcinoma (RCC) is an obesity-associated cancer. Adiponectin, a major adipocyte-secreted adipokine, plays anti-tumor properties in many malignancies, but exerted paradoxical actions on RCC. Herein, we investigated the effects of adiponectin on RCC progression and resistance to sunitinib, and to exploit this molecular mechanism. **Methods:** Tissues were collected from 126 patients with metastatic renal cell carcinoma (mRCC) treated with tyrosine kinase inhibitor (TKI) therapy. Tumor Adiponectine receptor 1 (AdipoR1) and Adiponectine receptor 2 (AdipoR2) were detected by immunohistochemistry. Assays with RCC cell lines were used to examine the signal transduction pathways of adiponectin in RCC. **Results:** AdipoR2 was generally lower expressed than AdipoR1 in mRCC tumor (15.6% vs 89.1%, $p < 0.001$). AdipoR1 expression, but not AdipoR2, was a significant independent predictor of favorable responding to TKI and good survival outcomes. In cultured RCC cells adiponectin inhibited migration and invasion of RCC cells and sensitized cells to killing by sunitinib. Mechanistic investigations of ligand-receptor interactions revealed that AdipoR1 could hinder migration and invasion of RCC cells by blocking GSK3β and β-Catenin pathway and increase cells sensitivity to sunitinib through inhibiting AKT and NF-κB pathway. However, AdipoR2 was not associated with the tumor-limiting properties of adiponectin. **Conclusions:** These results show that AdipoR1 is a potential prognostic marker for favorable outcomes of mRCC patients. Adiponectin-AdipoR1 axis could be a plausible target to impede tumor progression and sensitize tumors to TKI therapy.

635 **Poster Session (Board #H8), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM**

Does increasing time to surgery affect survival in stage I renal cell carcinoma? Analysis of the national cancer database.

Brittney Cotta, Stephen Ryan, Ahmed Eldefrawy, Reith Sarkar, Aaron Bradshaw, Margaret Frances Meagher, Zachary Hamilton, James Don Murphy, Ithaar Derweesh; University of California San Diego, San Diego, CA; University of California, San Diego School of Medicine, La Jolla, CA; Saint Louis University Department of Surgery - Urology Division, St Louis, MO

Background: Optimal timing for surgical treatment of localized renal cell carcinoma (RCC) remains undefined. We sought to determine the survival impact of time to definitive surgical treatment for Stage 1 RCC and elucidate factors associated with a delay in surgical care utilizing the National Cancer Database (NCDB). **Methods:** The NCDB was queried for Stage 1 RCC cases (cT1N0M0) from 2004-2013 treated with partial or radical nephrectomy. Quartiles were formed from the range of time to surgery of the entire cohort in days: early defined as the first two quartiles and delayed as the fourth. Descriptive analyses were conducted between early and delayed groups. Overall survival (OS) between early and delayed groups was calculated with Kaplan-Meier analysis. Multivariable analysis was performed to determine factors associated with delay in surgical care. **Results:** 38,859 patients were analyzed. Median time to treatment was 40 days (IQR 22-68). Early ($\leq$40 days, n = 23,712) and delayed ($>$ 68 days, n = 15,147) groups had a median follow-up of 44.8 and 41 months, respectively ($p < 0.001$). Delayed surgery was more frequent with African-Americans (14.8% vs. 9.1%, $p < 0.001$), patients with government or no insurance (53.7% vs. 45.1%, $p < 0.001$), males (60.7% vs. 58.3%, p = 0.001), and Charlson Comorbidity Index (CCI) $\geq$2 (9.7% vs. 6.7%, $p < 0.001$). Kaplan-Meier analysis demonstrated survival benefit to the earlier treatment group, with 5 year OS of 85.5% and 80.9% ($p < 0.001$; Figure). On multivariable analysis, increasing age (OR = 1.001, p = 0.015), African-American race (OR = 1.5, $p < 0.001$), increasing distance from treatment center (OR = 1.005, p = 0.001), residence in areas with low high school graduation rates (OR = 1.42, $p < 0.001$), residence in an area of $>$1 million population (OR = 1.6, $p < 0.001$), and CCI $\geq$2 (OR = 1.4, $p < 0.001$) were independently associated with increasing time to surgery. **Conclusions:** Surgery of T1 RCC carried out beyond 9 weeks after diagnosis is associated with reduced overall survival compared to patients treated within 6 weeks. Time to definitive surgical treatment should be a quality of care metric, with special attention given to populations most at risk for delays in care.

636 **Poster Session (Board #H9), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM**

Prevalence, disease-free (DFS) and overall (OS) survival of contemporary high-risk renal cell carcinoma (RCC) patients eligible for adjuvant checkpoint inhibitor trials: A RECUR database analysis.

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Background: Designing adjuvant trials is challenging because of uncertainties of prevalence and outcome of high-risk RCC despite use of validated risk scores. **Methods:** RECUR is a European multicenter database capturing patient and tumour characteristics, recurrence patterns and survival of all patients treated with (partial) nephrectomy for non-metastatic RCC from 2006 to 2011 at each participating center. We evaluated prevalence, DFS and OS of RCC according to eligibility criteria of adjuvant trials IMMotion 010 (NCT03024996, IM), Checkmate 914 (NCT03138512, CM), Keynote-564 (NCT03142334, KN) and RAMPART (NCT03288532, RP), which all predominantly recruited high-risk clear cell RCC patients. **Results:** Of 2669 relevant patients in RECUR, 424(15.9%), 681(25.5%), 579(21.7%) and 1221(45.7%) met eligibility criteria for IM, CM, KN and RP respectively ($p < 0.001$). Median DFS and OS estimates (Kaplan-Meier) in RECUR corresponding to each trial placebo arm were 37.5 (95%CI 30.4–44.6) and 89.6 (95%CI 76.1–103.0) months for IM, 89.4 (95%CI 66.1–112.7) and 96.2 (95%CI 79.8–112.6) months for CM, 62.6 (95% CI39.6–85.6) and 86.6 (95%CI 74.3–98.9) months for KN and finally at 144 months (DFS not reached) and 123.8 (95% CI 110.1 – 137.4) months for RP. Additionally, at pairwise analysis of evaluated trials, DFS estimates were significantly different between all trials ($p < 0.001$) except between CM and KN ($p = 0.125$), while OS estimates did not differ significantly between all trials except between RP and the other three trials ($p = 0.002$). **Conclusions:** Percentages of eligible high-risk RCC patients in RECUR were low to moderate and, together with estimated placebo arm DFS and OS, varied due to differences in trial eligibility criteria. These differences may impact on the results and interpretation of the trials.

637 **Poster Session (Board #H10), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM**

Direct impact of clinical research in metastatic renal cell carcinoma (mRCC): A cost-effectiveness analysis of patient care outcomes and cost savings in a real-life scenario of a large public university hospital in Spain.

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Background: Public health sustainability is a major concern worldwide. Clinical research is considered to leverage patient care outcome but also can lead costs savings and, subsequently, to maintain public health system. Thus, we analyzed the direct impact of clinical research in terms of improvement in clinical outcomes and costs related to research in patients with mRCC in real-life setting. **Methods:** We retrospectively collected data related to overall survival (OS) and direct health care costs from all mRCC patients who were treated with oral anti-tumour medication and followed at the Medical Oncology Department of Ramón y Cajal University Hospital in Madrid, between January 2010 and February 2017. A statistical analysis comparing the outcomes of patients included in clinical trials versus those not included was conducted. **Results:** In the study period, 65 patients were newly diagnosed with mRCC and received treatment. Those patients included in clinical trials showed higher median OS (91 vs. 29 months. HR 0.389; 95% CI: 0.150: 1.000; p=0.04). Median direct cost per mRCC patient in 'real-life' was €67,376. Median cost for a patient enrolled in at least one clinical trial was €53,673 vs. €63,834 for those who were never recruited for a trial. Participation in clinical trials contributed to a decrease in total health expenditure by 9.02% (€362,367), mainly due to reduction in the cost of medications and diagnostic tests (91.46% vs. 8.54%, respectively). Furthermore, clinical trial participants have required less number of hospitalizations (0.08 vs. 1.75) and emergency visits (0.39 vs. 3.2) per patient. **Conclusions:** Under the public health system perspective, participation in clinical trials is related to an improvement in overall survival as well as direct and indirect cost savings in mRCC patients.

639 Poster Session (Board #H12), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM

The association of NOX4 mediated nuclear colocalization and overall survival in renal cell carcinoma.

Dharam Kaushik, Hanzhang Wang, Keith A. Ashcraft, Alia Nazarullah, Michael A. Liss, Deepak Pruthi, Ahmed Mansour, Cooper B. Tye, Wasim Chowdhury, Dean Bacich, Denise O'Keefe, Ronald Rodriguez; University of Texas Health, San Antonio, San Antonio, TX; University of Texas, San Antonio, San Antonio, TX; University of Texas Health Sciences Center, San Antonio, San Antonio, TX

Background: NOX4 protein are involved in cell differentiation, migration and apoptosis. We recently demonstrated that NOX4 in renal cell carcinoma (RCC) is an energetic sensor and couples energy metabolism to drug-resistance. In this study we demonstrate that enhanced nuclear localization of NOX4 is correlated with poor survival. **Methods:** We identified 350 RCC patients with (n = 85) and without (n = 265) venous tumor thrombus (VTT) who underwent radical nephrectomy with or without thrombectomy at our institution between 2013-2016. Fifty patients with RCC and VTT were matched 1:1 to patients with RCC and no VTT. Tissue Microarray (TMA) consisting of primary renal tumor, adjacent renal tumor and VTT were created. These matched TMA (n = 174) were stained with NOX4 antibodies; scanned using the Aperio scanning system and analyzed with the ImageScope software. The RCC nucleus was evaluated for roundness, elongation and size. NOX4 nuclear staining was categorized based on intensity as either strong positive, moderate, weak or no localization. Differential protein expression between the primary tumor, adjacent normal parenchyma and VTT was assessed using the Chi-squared test or t-test. Progression-free survival (PFS) and overall-survival (OS), stratified by NOX4 staining intensity, was estimated using the Kaplan-Meier method and compared with the log-rank test. Cox regression model was used to investigate effect of NOX4 staining on survival in multivariate analyses. **Results:** NOX4 nuclear colocalization was higher in patients who had progression and death from RCC. On univariate analysis, the intensity of NOX4 protein expression in the nucleus was significantly associated with PFS (HR 1.67, 95%CI (1.08-2.57; p = 0.02) and OS (HR 2.31, 95%CI (1.26-4.24; p = 0.007). On multivariate analyses the association between NOX4 protein expression and OS remains statistical significance (HR 2.09, 95%CI (1.05-4.18, p = 0.037). **Conclusions:** We provide evidence that in high grade/high stage cancer, NOX4 is colocalized within the nucleus of RCC. The prognostic role of NOX4 was determined at the protein level. We provide rationale for further investigation of NOX4, which may serve as a checkpoint in RCC.

640 Poster Session (Board #H13), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM

Molecular stratification of high-grade unclassified renal cell carcinoma to improve prognostication and management strategy.

Yingbei Chen, Renzo G Di Natale, Gowtham Jayakumaran, Mazyar Ghanaat, Julian Marcon, A. Rose Brannon, Hikmat Al-Ahmadie, Samson Fine, Anuradha Gopalan, Sahussapont Joseph Sirintrapun, Satish Tickoo, Maria E. Arcila, Robert J. Motzer, A. Ari Hakimi, Victor E. Reuter; Memorial Sloan Kettering Cancer Center, New York, NY

Background: Unclassified renal cell carcinoma (uRCC) constitutes a large portion of aggressive non-clear cell RCC with limited response to standard therapy. Clinicopathologic parameters or biomarkers to stratify this heterogeneous group of tumors are currently lacking. In a recently reported analysis of 62 high-grade primary uRCC ["discovery cohort (DC)"], we identified distinct molecular subsets. We aimed to validate this molecular schema in an independent clinical cohort and further delineate the clinicopathologic and molecular features that may refine prognostication and management. **Methods:** All cases was reviewed by experienced GU pathologists based on the current WHO criteria. Primary (n = 54) or metastatic (n = 21) tumor samples from 75 uRCC patients ["validation cohort (VC)"] were analyzed by a CLIA-approved targeted NGS platform for somatic alterations. 37 had germline testing results available. We performed integrative analysis of both VC and DC. **Results:** Somatic mutations found in VC were *NF2* (24%), *SETD2* (13%), *SMARCB1* (9%), *TP53* (9%), *TSC1* (9%), *FH* (8%), *TSC2* (5%), *MTOR* (5%), *EP300* (5%), *BAP1* (5%), *PBRM1* (5%) and *PIK3CA* (5%), highly consistent with findings in DC. Germline alterations [*FH* (11), *SDHB* (4), and *SMARCB1* (1)] were detected in previously unsuspected patients. Integrative analysis supported the presence of NF2-loss (NF2), hyperactive mTOR-driven (MTOR), FH/SDH-deficient (FH/SDH), and chromatin/DNA damage response (Chrom/DDR) molecular subsets. Univariate analysis of combined DC and VC (n = 137, median f/u 26 mos, death 74%) showed a significantly higher risk associated with NF2 subset than the MTOR group (Table). Clonality analysis confirmed *NF2* inactivating mutation as a main driver in the NF2 subset. Rare cases with alterations indicating sensitivity or resistance to immunotherapy were also identified. **Conclusions:** Molecular features of high-grade uRCC improve risk stratification and provide rationale for distinct management strategies.

Molecular subset	VC (n)	Combined DC + VC (n)	HR (95% CI)	p value
MTOR	8	21	1	
NF2	14	29	2.56 (1.30 - 5.06)	0.01
Chrom/DDR	18	31	2.07 (1.04 - 4.15)	0.04
FH/SDH	18	22	2.37 (1.12 - 5.01)	0.02
Other	17	34	1.69 (0.87 - 3.28)	0.12

641 Poster Session (Board #H14), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM

Genomic biomarkers of response to nivolumab/ipilimumab (nivo/ipi) and nivolumab (nivo) monotherapy in 108 patients with advanced renal cell carcinoma.

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Background: Both the combination of nivo/ipi and nivo monotherapy have shown efficacy across multiple malignancies including clear cell Renal Cell Carcinoma (ccRCC). Biomarkers such as tumor mutation burden (TMB) are prognostic in other malignancies, however, remain unvalidated in ccRCC. This study investigates genomic biomarkers associated with nivo/ipi and nivo clinical response. **Methods:** Whole exome sequencing (WES) was performed on pretreatment tumor derived DNA from nivo/ipi and nivo treated patients from MSKCC and publicly available WES datasets (Miao D, Science, 2018, 359: 6377). Somatic mutations, TMB, neoantigen load (NA), and HLA zyogosity were correlated to objective response rate (ORR), progression free survival (PFS), and Overall Survival (OS). Alterations occurring in $<$ 10% of the cohort were considered non-evaluable (NE). **Results:** 108 patients had tumors studied; 32 patients with nivo/ipi and 76 patients with nivo therapy. No individual factors showed significant correlations to ORR or both PFS and OS. In the combined cohort, homozygosity at HLA-C was associated with shorter OS (HR=2.55 95% CI 1.17-5.57; P=0.02). In the nivo/ipi cohort, TMB (HR=0.36 95% CI 0.16-0.84; P=0.02) and NA (HR=0.43 95% CI 0.19-0.98; P=0.04) were associated with longer PFS. **Conclusions:** Increased TMB and NA load may predict for improved outcomes, and homozygosity at HLA loci may predict for worse outcomes. The predictors of response to nivo may not be generalizable to nivo/ipi. To rule out artifacts of multiple testing in a small cohort, validation in a larger dataset is necessary.

Hazard Ratio of Genomic Factors

	Increased TMB	Increased NA	HLA-C Homozygous	HLA-Any Loci Homozygous
Combined Cohort: N=108				
PFS	0.78; P=0.24	0.82; P=0.37	1.24; P=0.55	1.46; P=0.12
OS	0.85; P=0.62	0.77; P=0.41	2.55; P=0.02	1.66; P=0.13
Nivo/Ipi Cohort: N=32				
PFS	0.36; P=0.02	0.43; P=0.04	NE	2.52; P=0.15
OS	0.71; P=0.65	0.57; P=0.47	NE	3.22; P=0.16
Nivo Cohort: N=76				
PFS	1.06; P=0.82	1.16; P=0.56	1.12; P=0.76	1.13; P=0.65

642 Poster Session (Board #H15), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM

Patients' perspective of quality-of-life issues in a randomized study in open surgery of patients with renal cell carcinoma.

Britt-Inger Kroger Dahlin, Mascha Thurm, Ola Winso, Borje Ljungberg; Norrlands University hospital, Umea, Sweden; Norrlands University Hospital, Umea, Sweden; Umeå University, Umeå, Sweden

Background: This randomized study in patients treated with open surgery for renal cell carcinoma (RCC), aimed to evaluate if effective perioperative analgesia can be part of a multimodal approach to minimize morbidity and improve postoperative management [1]. To evaluate the patients' perspectives, a survey was used before surgery and one month after surgery. **Methods:** Between 2012 and 2015, 135 patients with RCC, in all stages, were randomized to receive either spinal analgesia with added clonidine, or epidural analgesia in addition to general anesthesia: The patients were stratified according to surgical technique. Inclusion criteria: ASA score $\leq$ III, age $>$ 18 years, and no chronic pain medication or cognitive disorders. The patient's survey used was based on the EORTC QLQ-C30 formula. Wilcoxon Signed Rank test and Mann-Whitney-U tests were used for statistical evaluation. **Results:** Most patients (117 of 135, 86 %) responded to the survey postoperatively. Patients groups treated with partial nephrectomy or radical nephrectomy both had significantly reduced physical and social functioning while emotional functioning improved postoperatively. In both surgical groups the patients reported significant negative financial difficulties. Similar results was achieved for patients treated with either spinal or epidural anesthesia. The epidural group of patients experienced more negative social functioning but had an improved global health. When comparing the surgical procedures there was no significant difference in the quality of life parameters. However when comparing the analgesic groups, spinal anesthesia had significantly better physical and social functioning while the patients in the epidural group reported better global health. **Conclusions:** In this randomized controlled study on nephrectomy, patients treated with spinal analgesia with clonidine, had better physical and social functioning postoperatively than patients treated with epidural analgesia. Clinical trial information: NCT02030717.

643 Poster Session (Board #H16), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM

The mutational burden of targeted genes significantly correlated with overall survival after targeted therapy in metastatic renal cell carcinoma.

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Background: This study aimed to find the correlation between tumor mutation burden and systemic first line therapeutic response in metastatic tissue samples from patients with metastatic renal cell carcinoma (mRCC). **Methods:** Between 2005 and 2017, 168 triplet-tissue block samples from 56 mRCC patients were selected for targeted gene sequencing (TGS) using the 88 targeted genes from the National Cancer Center, Korea (NCC) kidney cancer panel. The patients' medical records, including therapeutic responsive profiles with overall survival (OS) to first-line targeted therapy, were evaluated with the mutational burden of triplet tissue samples using 88 TGS. A few significant target genes associated with therapeutic response towards targeted therapy were identified after comparing the mutational burden of positive for all three blocks and one or two positive blocks (p-value < 0.05). **Results:** The median PFS for the first-line targeted therapy and OS were 8.7 and 42 months, respectively. MSKCC and Heng risk criteria showed 28.9/65.8/5.3% and 26,3/57.9/15.8% for favorable, intermediate, and poor risk groups, respectively. Also, 55.3% and 52.6% patients received metastatectomy and nephrectomy, respectively. Eighteen (32.1%) patients had all triplet blocks passed for quality check, whereas 21 (37.5%) and 17 (30.4%) patients had two or one passed tissue blocks, respectively. Among the 18 patients with triplet-block, TP53, URB4, PTK2, and SGO2 genes had significant discrimination power for OS on comparing their mutational burden in the three blocks positive group (N = 7) and two or fewer blocks positive groups (N = 11) ($p < 0.05$). Among the 39 patients with either doublet or triplet blocks passed for quality check, TP53, URB1, PTK2, SGO2, BRAF, NEDD4, PDXDC1, CDH1, FGFR2, RET, RUNX1, and SDHB genes had significant discrimination power for DFS when comparing their mutational burden in the three blocks positive group (N = 7) and two or fewer blocks positive groups (N = 14) ($p < 0.01$). **Conclusions:** The study showed the tumor mutational burden of many vital targeted genes to be significantly correlated with OS from metastatic tissues in mRCC.

644 Poster Session (Board #H17), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM

Influence of access on survival of renal cancer in a Brazilian center.

Luciana de Moura Leite, Aldo A. Dettino, José Augusto Rinck, Stenio Cassio Zequi, Simone Loose, Maria Nirvana Cruz Formiga; A.C. Camargo Cancer Center, São Paulo - SP,, Brazil; A.C. Camargo Cancer Center, São Paulo, Brazil; A.C.Camargo Cancer Center, São Paulo, Brazil; A.C. Cancer Center, São Paulo, Brazil

Background: The introduction of tyrosine kinase inhibitors (TKI) and recently immunotherapy has brought major survival benefits for metastatic renal cancer (mRCC) patients (pts). In Brazil, there is no approved 2nd line treatment for mRCC in the Public Health System (PHS). Our center is unique, because it provides care for both PHS and Private System (PrS) population, enabling us to make the comparison of overall survival (OS) of these pts. **Methods:** We retrospectively reviewed medical records of all mRCC pts treated with 1st line TKI at our service from 2007 to 2018. Categorial variables were compared by Fisher's exact test and continuous by Mann–Whitney. Survival was estimated by Kaplan-Maier method, prognostic factors adjusted by Cox regression model. **Results:** 171 pts were eligible, 37 (21.6%) PHS and 134 (78.4%) PrS pts. Between the two groups, there was no differences in age, gender, number and sites of metastasis (mets). PHS pts had worst ECOG (≥2, in 35.1 vs 13.5%, p .007), a trend towards more poor IMDC risk (IMDC favorable 16.2 vs 26.6%, intermediate 51.4 vs 57%, poor 32.4 vs 16.4%, p.09), had less nephrectomies (73 vs 92.5%, p.008) and more non clear cell histology (32.4 vs 12.7%, p.01). Median lines of therapy were 1 for PHS vs 2 for PrS pts (p.03). Sunitinib was the 1st line agent for 91.9 vs 67.2%, and pazopanib 8.1 vs 29.9%, of the PHS and PrS pts, respectively. Median time from diagnosis of mets to treatment start was 2.29 vs 1.79 m (p.59). Median OS was 16.5 vs 26.5 m (p.0002) and progression free survival, 8.4 vs 11 m (p.01), for the PHS vs PrS. On multivariate analysis, after adjusting for factors that were present before the beginning of treatment and were statistically significant for OS in the univariate model, PHS pts still had higher risk of death (HR 1.85, IC 95 1.2-2.9, p.01), probably due to having received fewer lines of therapy (≥2 lines of therapy vs 1, HR 0.51, IC95 0.4-0.7, p .001). **Conclusions:** Brazilian PHS pts had significant worse OS compared to PrS pts, in part due to less access to drugs. Access to cancer drugs is a challenge worldwide, and in Brazil effort has to be done to change this reality.

645 Poster Session (Board #H18), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM

Immune-related adverse events are associated with improved outcomes in ICI-treated renal cell carcinoma patients.

Roy Elias, Flora Yan, Nirmish Singla, Nicholas Levonyack, Joseph Formella, Alana Christie, Payal Kapur, Alex Isaac Bowman, Hans J. Hammers, Raquibul Hannan, James Brugarolas; University of Texas Southwestern Medical Center, Dallas, TX; Kidney Cancer Program, Simmons Comprehensive Cancer Center, University of Texas Southwestern Medical Center, Dallas, TX

Background: With the approval of immune-checkpoint inhibitors (ICI) as first and second line agents for treating metastatic renal cell carcinoma (RCC), immune-related adverse events (irAE) are a growing concern. In this study, we present the safety profile and outcomes of 90 patients with RCC treated at two centers, including a university (UT Southwestern/Clements University Hospital) and a county hospital (UT Southwestern/Parkland). **Methods:** All patients with RCC treated with ICI were identified from 2013 to January 31, 2018. We examined the incidence of any treatment-related adverse events and "select" irAEs and evaluated their impact on patient outcomes and therapeutic decisions. Kaplan-Meier methods and Cox proportional hazards regression models were used to compare overall survival (OS) and time to next therapy (TTNT) by the presence of irAEs. **Results:** Of 90 patients treated with ICI, 65 (72.2%) patients experienced adverse events, most commonly fatigue (37.8%), nausea (14%), and decreased appetite (12.2%). Select irAEs were seen in 38 (42.2%) with the most common irAEs involving the skin (15.6%), gastrointestinal tract (14%), endocrine organs (11%), and lungs (7.8%). There were 15 (16.7%) grade III/IV irAEs resulting in cessation of therapy for 12 (13.3%) patients. The median OS was 35.9 (95% CI: 24.3-not reached) and 26.5 months (95% CI: 10.2-28.8; p = 0.002) for patients with and without irAEs, respectively. The median TTNT was 17.8 (95% CI: 11.3-29.3) and 6.6 months (95% CI: 4.5-9.6; p = 0.002) for patients with and without irAEs, respectively. In multivariate analysis of irAE status and Heng prognostic score, irAEs were associated with improved OS, HR 0.376 (95% CI 0.179–0.792; p = 0.010) and TTNT, HR 0.482 (95% CI 0.280–0.829; p = 0.008). **Conclusions:** ICI in RCC is well tolerated with only 16.7% of patients experiencing an adverse event resulting in cessation of therapy. The development of an irAE correlated with both an improved median OS as well as median TTNT, a benefit that persisted after multivariate analysis including Heng prognostic scoring. These findings suggest that the development of irAEs may be an independent positive prognostic factor in patients with RCC treated with ICI.

646 Poster Session (Board #H19), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM

Results of a phase II study to evaluate the safety and efficacy of RX-0201 in combination with everolimus in subjects with metastatic renal cell carcinoma (mRCC).

Neeraj Agarwal, Sumanta K. Pal, Richard C. Lauer, Gurkamal S. Chatta, Sanjay Goel, Parminder Singh, Srinath Sundararajan, Callie Heaton, Christine Peterson, Ely Benaim, Scott T. Tagawa; Huntsman Cancer Institute at the University of Utah, Salt Lake City, UT; City of Hope, Duarte, CA; University of New Mexico Comprehensive Cancer Center, Albuquerque, NM; Virginia Mason Medical Center, Seattle, WA; Montefiore Medical Center, Albert Einstein College of Medicine, Bronx, NY; University of Arizona Cancer Center, Tuscon, AZ; University of Arizona Cancer Center, Tucson, AZ; Rexahn Pharmaceuticals, Inc., Rockville, MD; Division of Hematology & Medical Oncology, Meyer Cancer Center, Department of Urology, Weill Cornell Medical College & New York-Presbyterian Hospital, New York, NY

Background: RX-0201 is a novel 20-mer oligonucleotide that binds to mRNA coding for AKT-1, preventing AKT-1 expression and limiting the amount of downstream p-AKT. In vitro RX-0201, in combination with everolimus, additively inhibited Caki-1 cell growth. RX-0201, in combination with everolimus, to treat mRCC was evaluated in a Phase 1b/2 clinical study. **Methods:** This Phase 1b/2 study (2-stage design, NCT02089334) evaluated the efficacy and safety of RX-0201 in combination with everolimus in eligible subjects with mRCC. Eligible subjects must have had confirmed histologic or cytologic evidence of renal cancer with a clear cell component, measurable disease as defined by RECIST, received at least 1 course of therapy with a VEGFR inhibitor and progressed within 6 months of planned first dose of on study treatment. In Phase 1 subjects were enrolled at increasing doses of RX-0201 (delivered via continuous IV for 14 days) in combination with 10 mg/ day everolimus in a modified 3+3 design. The target dose of RX-0201 identified in Phase 1, 250 mg/ m^2/day, was further evaluated in Phase 2. Primary objectives included the safety and efficacy at the recommended Phase 2 dose. The Phase 2 primary endpoint was progression free survival (PFS) benefit for at least 4.5 months. **Results:** Eleven subjects (7 males, 4 females) with mRCC were treated with RX-0201 (250 mg/m^2/day) + everolimus (10 mg/ day) in Phase 2. The median age was 63 years, ECOG performance status at screening was 0 to 1, and 55% received $\geq$ 3 prior therapies. The median PFS in evaluable subjects was 4.9 months. Four subjects had stable disease after 6 months of treatment. The most frequent related adverse events ($>$ 15%) were G1/2 epistaxis, G3 fatigue, G1/2 nausea and G1 vomiting. **Conclusions:** In this mRCC population with extensive prior therapy, RX-0201 in combination with everolimus was safe, well-tolerated, and showed promising efficacy. The results also support the therapeutic significance of the AKT-1/mTOR pathway in mRCC. Clinical trial information: NCT02089334.

647 Poster Session (Board #H20), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM

Prognostic and predictive role of comprehensive geriatric assessment (CGA) in elderly patients with metastatic renal cell cancer (RCC) treated with sunitinib (SUN) or pazopanib (PAZ): A single center experience.

Francesco Pierantoni, Umberto Basso, Marco Maruzzo, Antonella Brunello, Giuseppe Anile, Annunziata Lettiero, Giuseppina Tierno, Evelina Lamberti, Vittorina Zagonel; Oncologia Medica 1 - Istituto Oncologico Veneto IOV - IRCCS, Padova, Italy; Istituto Oncologico Veneto IOV - IRCCS, Padova, Italy; Istituto Oncologico Veneto - IOV, Padova, Italy; Istituto Oncologico Veneto, IRCCS, Padova, Italy; Oncology Unit 1, Istituto Oncologico Veneto IOV IRCCS, Padova, Italy; Medical Oncology Unit 1, Istituto Oncologico Veneto IOV IRCCS, Padova, Italy; Department of Clinical and Experimental Oncology, Medical Oncology 1, Veneto Institute of Oncology, IOV-IRCCS, Padua, Italy

Background: Few data are available concerning the prognostic and predictive role of CGA in elderly pts ≥70 years with metastatic RCC treated with either Sun or Paz. **Materials and Methods:** We retrospectively reviewed the charts of all elderly pts with advanced RCC treated at our Institute with either Sun or Paz, with at least 6 months follow-up after starting treatment. Every pt received at baseline a CGA and was classified as fit, vulnerable or frail according to Balducci's Criteria. **Results:** We identified 73 pts who started therapy from January 2006 to March 2018, median age 76 years (range 70-89), 63% males; 42.5% fit and 57.5% unfit pts (38.3% vulnerable, 19.2% frail). Sun to Paz ratio was 40 to 33 pts with a median duration of treatment of 10.8 months; incidence of G1/2 toxicities was 85% vs 93.9% (p = 0.28), G3/4 was 37.5% vs 30.3% (p = 0.63), dose reduction was necessary in 77.5% vs 78.8% of pts (p = 0.9), respectively. Median PFS and OS with Sun or Paz were 13.6 vs 9.4 months (p = 0.152) and 27 vs 22.3 months (p = 0.641), respectively. CGA fit category predicted longer PFS (p = 0.039) and OS (p = 0.001) in the whole cohort. We found no significant differences between fit and unfit pts according to incidence of G1/2 adverse events, incidence of dose reduction or necessity to early suspend treatment due to toxicity, while the incidence of G3/4 events was lower in the fit subgroup (p = 0.026). Out of 67 pts progressing after first line therapy, 27 (40.3%) received a second line consisting in Nivolumab (22.4%), Everolimus (13.4%) and Sorafenib (4.5%), while 40 (59.7%) received only palliative treatments. CGA fit category significantly correlated with a higher chance of receiving a second line treatment (p = 0.004). **Conclusions:** In our retrospective single-center experience, CGA has a strong prognostic value in terms of OS and has the ability to discriminate pts at higher risk of experiencing G3/4 toxicities with Sun or Paz, with shorter PFS and lower chance of receiving a second line treatment. There were no striking differences in terms of toxicity rates between Sun or Paz, although different in type and possibly biased by patient selection.

648 **Poster Session (Board #J1), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM**

Treatment disparities among patients in the National Cancer Database (NCDB) with clinical TIa and TIb renal masses.

Joshua Sterling, Zorimar Rivera-Nunez, Nicholas Farber, Parth K. Modi, Kushan Dilip Radadia, Sinae Kim, Goyal Sharad, Parikh Rahul, Robert E. Weiss, Isaac Kim, Sammy Elsamra, Thomas Jang, Eric Singer; Rutgers Robert Wood Johnson Medical School, Division of Urology, New Brunswick, NJ; Rutgers Cancer Institute of New Jersey, Department of Radiation Oncology, New Brunswick, NJ; Rutgers Cancer Institute of New Jersey, Rutgers Robert Wood Johnson Medical School, New Brunswick, NJ; Rutgers Cancer Institute of New Jersey, Division of Radiation Oncology, New Brunswick, NJ; Rutgers Cancer Institute of New Jersey, Piscataway, NJ; Section of Urologic Oncology, Rutgers Cancer Institute of New Jersey, New Brunswick, NJ; Rutgers Cancer Institute of New Jersey, New Brunswick, NJ

Background: AUA guidelines on the management of renal cell carcinoma (RCC) recommend prioritizing partial nephrectomy (PN) for the treatment of clinical T1a (cT1a) tumors, using PN for clinical T1b (cT1b) tumors when feasible, and performing minimally invasive surgery (MIS) when possible. Since cT1 RCC is a heterogeneous disease, we evaluated patterns of care in this population to examine factors associated with receipt of PN and MIS. **Methods:** We queried the NCDB from 2010-2014 to identify patients treated surgically for cT1N0M0 RCC. Patient socio-demographics, clinical characteristics, and treatment parameters were compared between cT1a and cT1b patients. Logistic regression models examined factors associated with receiving MIS. **Results:** Our population included 69,694 patients (44,043 cT1a and 25,651 cT1b). For cT1a tumors, 70% of patients received PN, while 30% received RN; 35% of patients underwent an open procedure and 65% underwent MIS. For cT1b tumors, 32% of patients received PN and 68% received RN; 38% of patients underwent an open operation and 62% underwent MIS. In both cohorts, African Americans and those earning <$62,000 were less likely to have MIS. Distance to treatment was not significant in cT1b patients, but cT1a patients who traveled >31 miles were more likely to undergo MIS. Patients treated at a community hospital were less likely to receive MIS compared to those treated at academic centers (cT1a OR: 0.48, 95% CI: 0.44-0.53 and cT1b OR: 0.63, 95% CI: 0.56-0.7). cT1a patients without private insurance were less likely to receive MIS (OR range: 0.58-0.93). However, only uninsured cT1b patients were less likely to undergo MIS (OR: 0.74, 95% CI: 0.64-0.86). **Conclusions:** PN occurred more frequently for cT1a (70%) vs. cT1b (32%) tumors. Most cT1 tumors received MIS; 35% of cT1a patients and 38% of cT1b patients underwent an open procedure, presenting an opportunity for improvement. cT1a and cT1b patients with lower household income, without private insurance, and those treated outside academic centers were less likely to receive MIS. Based on these findings additional research on the impact of regionalization of RCC surgery on utilization of PN vs. RN, receipt of MIS, and outcomes is warranted.

649 **Poster Session (Board #J2), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM**

Effect of immunotherapy (IO) on primary renal tumor in metastatic renal cell cancer (mRCC).

Antoine Jamet, Caroline Caramella, Annalisa Guida, Julia Arfi-Rouche, Zahira Merabet, Emeline Colomba, Bernard Escudier, Laurence Albiges; Institut Gustave Roussy, Villejuif, France; Radiology Department, Gustave Roussy, Villejuif, France; Gustave Roussy Cancer Institute, Villejuif, France; Gustave Roussy Cancer Campus, Paris Saclay University, Villejuif, France; U1015 INSERM, Gustave Roussy Cancer Campus, Paris Saclay University, Villejuif, France; Medical Oncology, Gustave Roussy, Université Paris-Saclay, Villejuif, France, Villejuif, France

Background: Recent data showed that cytoreductive nephrectomy (CN) should not be performed prior to systemic therapy in intermediate and poor risk groups. Immune checkpoint inhibitors (ICI) are now approved in first and second line in mRCC, but ICI effect on the primary tumor is unknown. **Methods:** All patients (pts) treated with ICI for mRCC without prior CN were retrospectively collected and sequential computed tomography (CT) scan evaluated for response. Primary objective was Objective Response Rate (ORR) in the primary renal tumor in the primary RECIST 1.1. Secondary objective included systemic ORR and nephrometry score changes. **Results:** A total of 20 pts were treated with ICI with primary tumor *in situ* between 12/2012 and 10/2018. Among these, CT scans were available for evaluation of response for 19 primary tumors in 18 pts. Median age was 59.5 years. Pathology was 16 clear cell RCC, 2 translocation RCC, 1 Collecting duct carcinoma. Baseline median primary renal tumor size was 7.3 cm. ICI was used in first line setting in 7 pts, in second line or beyond in 13 pts. IMDC risk group at ICI start was favourable in 2 pts, intermediate in 9 pts and poor in 9 pts. ICI used was NIVOLUMAB(N) single agent in 13 pts or in combination in 7 pts (6 N-IPILIMUMAB and 1 N-VEGFRTKI). After a median follow up of 6.5 month from ICI start and a median duration of immunotherapy of 3.0 month, ORR on the primary tumor, was 3/19 (16%) (1 CR and 2 PR), 14 tumors (74%) were stable, and 2 had PD as best response. Median change in primary renal tumor was -1%. ICI use did not change nephrometry score. At extra renal assessment, ORR (systemic) was 5/18 (28%), (2 CR, 3 PR), 5 (28%) SD, and 8 (44%) PD (including 1 with new lesion and 1 with non-target lesion PD). Interestingly, 4 pts/18 (22%) had mixed response with opposite response between primary and systemic response. Furthermore, 11/18 (61%) would not classified in same RECIST group (CR, PR, SD, PD) between primary and metastatic sites assessment. **Conclusions:** To our knowledge, we report the first cohort of patients treated with ICI investigating the response on the primary tumor. ICI can induce a significant reduction in primary renal tumor, especially complete response and therefore raise the question of delayed CN in responders under ICI.

650 Poster Session (Board #J3), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM

Sunitinib for metastatic renal cell carcinoma: A systematic review and meta-analysis of real world and clinical trials data.

Michael Moran, Dana J. Nickens, Katherine Adcock, Arial Desscan, Meg Bennetts, Natalie Charnley, Kate Fife; Pfizer Inc., London, United Kingdom; Pfizer Inc., La Jolla, CA; Pfizer Global, London, United Kingdom; Pfizer R&D UK Ltd, Sandwich, United Kingdom; Lancashire Teaching Hospitals, Preston, United Kingdom; Cambridge University Hospitals NHS Foundation Trust, Cambridge, United Kingdom

Background: Randomized controlled trials (RCTs) are the basis of approval for medical interventions, but may not fully reflect populations seen in clinical practice. Sunitinib is a widely used 1st-line treatment for patients (pts) with metastatic renal cell carcinoma (mRCC). This is the first large-scale meta-analysis to evaluate the efficacy of sunitinib using the novel approach of combining RCTs and real-world data (RWD). **Methods:** PubMed, Ovid, MEDLINE and EMBASE were searched from 2000-2017 for RCTs and RWD studies of sunitinib as 1st-line treatment in pts with mRCC. Eligible studies contained a cohort of ≥50 adult pts per study arm. The meta-analysis combined RWD and RCT study arms, adjusting for data type (RCT or RWD). Recorded outcomes were: median progression-free survival (mPFS), median overall survival (mOS) and objective response rate (ORR). A random effects model to account for study heterogeneity was applied to each endpoint. Sensitivity analyses evaluated the robustness of the overall estimate. **Results:** Of the studies that met eligibility criteria, mPFS, mOS and ORR were reported by 18, 19 and 15 studies, respectively. Combined RWD and RCT analyses are presented in the Table. Reported mPFS (RWD, 7.5–11.0; RCTs, 5.6–15.1 months) and ORR data (RWD, 14.0–34.6%; RCTs, 18.8–46.9%) were consistent with the overall estimates. Reported mOS showed greater variation in RWD (6.8–33.2 months) compared with RCTs (21.8–31.5 months). Sensitivity analyses showed no evidence of lack of robustness for mPFS, mOS or ORR. Interpretation of these results is limited by differences in trial design and cohort characteristics. **Conclusions:** This novel, large-scale meta-analysis validates sunitinib as an effective 1st-line treatment for pts with mRCC in both RCTs and everyday clinical practice.

	Studies, n (RWD, RCT)	Pts, n (RWD, RCT)	Confidence estimate, months (95% CI)
mPFS	18 (11, 7)	4815 (3098, 1717)	9.3 (8.6-10.2)
mOS	19 (14, 5)	5321 (3972, 1349)	23.0 (19.2-27.6)
ORR	15 (10, 5)	4183 (2694, 1489)	27.9 (24.2-32.0)

CI, confidence interval; RCT, randomized controlled trial; RWD, real-world data.

651 Poster Session (Board #J4), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM

Leveraging a robust patient-derived xenograft platform to characterize predictors for engraftment and oncologic outcomes in renal cell carcinoma patients.

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Background: Patient-derived xenograft (PDX) models of renal cell carcinoma (RCC) preserve the biological features of patient tumors, providing a platform for biomarker identification and preclinical drug testing. We sought to identify predictors of successful tumor engraftment and evaluate the prognostic value of engraftment in patients with RCC using a robust murine PDX platform. **Methods:** 1,200 specimens derived from nephrectomy, thrombectomy, metastasectomy, or biopsy were orthotopically (renally) implanted into NOD/SCID mice between 2008-2018. Non-RCC pathology was excluded. Stable engraftment was defined by successful passage of tumor tissue at least twice with histologic confirmation. Clinicopathologic characteristics were stratified by engraftment status, and multivariate (MVA) logistic regression was used to identify predictors of engraftment. Kaplan-Meier and Cox regression analyses were used to assess the prognostic value of engraftment on patient overall (OS) and disease-free (DFS) survival. **Results:** 1,003 independent PDX lines derived from 770 RCC patients were included. 157 (15.6%) lines successfully engrafted and exhibited higher tumor grade, stage, size, and presence of sarcomatoid or rhabdoid components. Whole exome sequencing was performed on 230 PDX lines. On MVA, sarcomatoid (OR 5.71, $p < 0.001$), rhabdoid (OR 2.79, $p = 0.046$), and advanced stage (OR 1.72, $p = 0.049$) were significant predictors for engraftment, while high grade and metastatic tumor source were significant only on UVA. Engraftment was associated with poor OS (HR 2.11, $p < 0.001$) and DFS (HR 1.85, $p = 0.020$) in patients after controlling for sarcomatoid, rhabdoid, grade, stage, and age on MVA. **Conclusions:** Aggressive RCC biology correlates with successful engraftment in PDX models. Engraftment remains independently predictive of OS and DFS even after controlling for adverse pathologic features. Engraftment in mice may illuminate aspects of tumor biology not captured by clinicopathologic variables and provide insight into novel determinants of tumor aggressiveness and metastasis. Efforts are underway to elucidate genomic drivers of engraftment.

652 Poster Session (Board #J5), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM

Safety and efficacy of restarting immune checkpoint inhibitors (CPI) after immune-related adverse events (irAEs) in metastatic renal cell carcinoma (mRCC).

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Background: CPI can induce a range of irAEs with various degrees of severity. Clinical experience with retreatment following clinically significant irAEs is growing. **Methods:** We retrospectively reviewed mRCC patients treated with CPI-based regimens who had >1 week therapy delay for irAEs at Dana Farber and Emory to characterize the safety and outcomes of retreatment. Toxicity was graded by CTCAEv5. Patients were divided into retreatment (R) and discontinuation (D) cohorts. Patient characteristics were compared by Fisher's exact test or Wilcoxon's rank sum test. ORR, OS and PFS were assessed descriptively. **Results:** Of 339 treated with CPI, 53 (16%) had irAEs warranting treatment interruption: 24 (45%) in R and 29 (55%) in D. Median (med) time to drug interruption was 2.0 (<0.1-74) months (mos) in D and 3.2 (<0.1-21) mos in R (p=0.89). Prior to irAE onset, 8 (28%) of cohort D and 5 (21%) of cohort R experienced partial responses (PR). While type of irAEs were balanced across D and R, initial irAEs were less severe in R vs D (all p<0.05) with fewer grade (gr) 3-4 events (29% vs 66%), less hospitalizations (25% vs 69%), and lower steroid requirements (>40 mg: 29% vs 79%). The most common irAEs in R were transaminitis, pancreatitis and dermatitis with 7 gr 3/4 events (pancreatitis, colitis, adrenal insufficiency and dermatitis). Median drug break before retreatment was 1.2 (0.3-4.8) mo. Subsequent irAEs occurred in 42% (n=10) after restarting (8 new, 2 recurrent) with 2 discontinuations; 6/10 were gr 3 with no gr 4/5 events. Median interval to irAE recurrence after retreatment was 2.1 (0.5-3.3) mos. Retreatment resulted in 4 (17%) PRs in patients whose disease had not responded prior to irAE (med time to PR from R = 2 mos). **Conclusions:** Despite a significant rate of irAE recurrence, most patients with prior clinically significant irAEs can be safely retreated. Retreatment can induce responses in an appreciable proportion of patients with no response prior to irAE. Larger studies are warranted to confirm these findings.

	D(N=29)	R(N=24)
ORR	10 (35%)	9 (37%)
Med PFS, mos (95%CI)	10.3(5.5-28.8)	12.2(7.6-23.5)
No. deaths	12(41%)	8(33%)
18mos OS rate (95%CI)	69%(47-83%)	78%(54-90%)

653 Poster Session (Board #J6), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM

Safety and efficacy of immune checkpoint inhibitors (CPI) in metastatic renal cell cancer (RCC) and urothelial cancer (UC) patients (pts) with pre-existing autoimmune disorders (AD).

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Background: The pivotal clinical trials of CPI generally excluded pts with AD given concern for serious exacerbations. There is limited data on the safety and efficacy of CPI in this population. **Methods:** We conducted a retrospective single center analysis of RCC and UC pts treated with CPI. Pts were grouped by presence or absence of AD. We catalogued the incidence of new irAEs (CTCAEv4), AD exacerbations, objective response rate (ORR, RECIST 1.1), and overall survival (OS, Kaplan Meier). Competing risk models estimated cumulative incidences of irAEs and CPI discontinuation using 6 months (mos) as a benchmark. **Results:** 271 RCC and 220 UC pts were identified. Median followup was 21 mos for RCC and 13 mos for UC. 25 (9%) RCC and 27 (12%) UC had pre-existing AD; most commonly dermatologic and rheumatologic. A minority (3% RCC/4% UC) had clinically active AD requiring concurrent immunomodulators. AD exacerbations occurred in 8 (32%) RCC and 12 (44%) UC; median time to exacerbation was 86 (25-270) and 27 (8-300) days, respectively. Cumulative incidence of new irAEs at 6 mos was numerically higher in RCC AD pts (50% vs 37%). CPI discontinuation and clinical outcomes were similar among AD and non-AD pts (Table). **Conclusions:** CPI are active in advanced RCC and UC pts with pre-existing AD. Exacerbations and new irAEs should be expected, but AD pts can experience similar outcomes and rates of drug discontinuation. Larger scale investigations are warranted.

	RCC			UC		
	AD	No AD	p	AD	No AD	p
N	25	246		27	193	
AD Exacerbation, N (%)						
-Overall	8(32)	-		12(44)	-	
-Grade 3/4	1(4)	-		4(15)	-	
New irAE, N (%)						
-Overall	12(48)	107(44)		9(33)	66(34)	
-Grade 3/4	2(8)	30(12)		3(11)	20(10)	
Cumulative incidence at 6mos, % (95%CI)*						
-New irAE	50(28-69)	37(31-43)	0.69	27(11-45)	33(26-40)	0.64
-CPI Discontinuation						
->For toxicity	12(3-29)	8(5-12)	0.84	16(5-32)	6(3-10)	0.48
->For progression	40(21-59)	39(32-45)	0.72	47(27-65)	56(48-63)	0.17
ORR, %(95%CI)	44(24-65)	31(25-37)	0.18	42(22-63)	32(24-39)	0.35
2yr OS, %(95%CI)	54(31-72)	55(47-63)	0.79	52(24-74)	35(26-44)	0.11

*Gray's test. CPI discontinuation for progression and other reasons were considered competing risks.

654 **Poster Session (Board #J7), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM**

Relation between clinicopathological findings and PD-1 or PD-L1 status in non-clear cell renal cell carcinoma by a multicenter study.

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Background: We investigated correlation of their pathological findings and their prognostic factors in non-clear cell renal cell carcinoma (ncRCC) diagnosed by both regional pathology (RP) and central pathology (CP) in multicenter study. **Methods:** In January 2005 to December 2014, 140 cases of ncRCC diagnosed by radical or partial nephrectomy were assessed. We assessed their pathological diagnosis by one central pathologist using the 2016 WHO classification tumor of the kidney. We assessed the correlation between clinical parameters or pathological findings and their prognosis. Then, we performed immunohistochemical analysis using PD-1 related antibody in ncRCC. **Results:** Median follow up was 32.7 months (1-134). Median age was 66 years, 99 males and 41 females. Pathological stage was pT1a: 58, pT1b: 30, pT2a: 17, pT2b: 6, pT3a: 21, pT3b: 2, pT4: 3 cases, respectively. In RP, histology was papillary (PAP): 60 (42.9%), chromophobe (CHR): 49 (35.0%), containing with sarcomatoid components (SAR): 14 (10.0%) and other histology: 17 (12.1%) cases, respectively. The tumors evaluable by CP were 127 cases, PAP: 52 (40.9%), CHR: 31 (24.4%), SAR: 20 (15.7%) and other histology: 24 cases (18.8%), respectively. The overall concordance rate was 59.5% between RP and CP. In multivariate analysis, SAR was extremely poor prognosis in ncRCC. The high neutrophil lymphocyte ratio (NLR) and at high CRP value were also poor prognostic factors. So, we stratified three risk groups using three factors, namely NLR, CRP and SAR. In overall survival, there were significant prognostic differences within three groups ($p = 0.0014$). In immunohistochemistry, PD-1 or PD-L1 expression correlated with poor overall, cancer specific and recurrence free survival in ncRCC. In multivariate analysis, PD-L1 expression was most significant prognostic factor for ncRCC. **Conclusions:** These results suggest that Risk stratification by three risk factors is useful prognostic model and the expression of PD-1 and PD-L1 may be a useful prognostic factor in ncRCC.

655 Poster Session (Board #J8), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM

Cell-free DNA analysis in renal cell carcinoma: Comparison with tumor sequencing and correlation with response to therapy.

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Background: Massively parallel sequencing (MPS) of circulating-free DNA (cfDNA) is seeing increasing use in multiple cancer types. There is little data on its use in metastatic renal cell carcinoma (mRCC) as a tool for prognostication and disease monitoring. **Methods:** cfDNA was extracted from 63 blood samples of 40 metastatic RCC patients (pts). Serial samples were obtained in 12 of 40 (30%) pts (median = 1, range = 1-7). cfDNA was used for targeted MPS using a custom bait-set of 27 genes commonly mutated in RCC. Variants observed in at least 3 reads, in both read directions, and at an allele frequency (AF) of $\geq$0.5% for single nucleotide variants (SNV), or in 2 reads and AF of $\geq$0.2% for small indels, were candidate variants validated by Sanger sequencing or amplicon MPS (aMPS). All mutations identified in cfDNA were also assessed in matched patient WBC DNA using aMPS and Sanger sequencing. Tumor specimens from 23 pts were also sequenced in parallel using our institutional OncoPanel assay that assesses 275-447 cancer-associated genes and results were compared with those seen in the cfDNA. **Results:** Thirty-one of 38 (82%) candidate variants were validated in 17 of 40 pts. Ten of those (32%) from 10 pts were also detected in WBC DNA, 3 of which were germline and 7 were at low mosaic frequency and likely reflected clonal hematopoiesis (CH). The remaining 21 variants validated in cfDNA were in *TP53* (6), *PBRM1* (3), *SETD2* (3), *VHL* (2), *ATM* (2), *NF2* (2), *PTEN* (1), *PIK3CA* (1), and *MTOR* (1). Two of 17 (12%) pts without tumor mutation analysis had 4 validated variants seen in cfDNA only. 10 of 23 (43%) pts with tumor mutation analysis had one or more variants seen in both tumor DNA and cfDNA. Three of the 23 had mutations seen only in cfDNA. Pts with any mutation in cfDNA (n = 14) had a significantly shorter overall survival in comparison to those without a finding ($p < 0.001$). Among 12 pts with serial samples, 5 had cfDNA variants identified. Response to therapy correlated with variant prevalence in all 5, including 2 with significant partial responses. **Conclusions:** This study suggests that paired tumor–cfDNA analysis has value in the assessment of response to therapy in RCC. Further analysis is proceeding.

656 Poster Session (Board #J9), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM

A multigene expression score for predicting response to anti-PD-1/PD-L1 therapy for clear cell renal cell cancer patients.

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Background: Anti-PD-1 inhibitor nivolumab and combination checkpoint inhibition (nivolumab and ipilimumab) are approved for advanced clear cell renal cell cancer (ccRCC), with objective response rates between 25% to 40%. PD-L1 expression is a poor predictor of anti-PD-1/PD-L1 therapy response in ccRCC. Better predictive biomarkers are required. The CLEAR score (CS) is a multigene prognostic expression score for ccRCC (Eur Urol 2015) previously associated with TKI outcomes. Given association of prognosis and clinical benefit, CS was explored as a biomarker for response to anti-PD-1/PD-L1 therapy in this study. **Methods:** CS is derived from the expression of 8 genes in ccRCC tumor tissue and intervening stroma and includes components of chemokine signaling. Based on this, immunohistochemistry of ccRCC tumor tissue (n = 24; matched CS also derived from same tissue), was done for tumor-infiltrating lymphocytes (CD8+) and PD-L1. Staining intensity was also correlated to CS. In another set of RCC patients who received nivolumab or pembrolizumab after progression on anti-angiogenic therapy (n = 12), correlation of their tumor CS and response outcome to anti-PD-1 therapy was done. **Results:** CS was significantly higher for ccRCC tumors with higher intratumor and/or stromal CD8+ cell infiltration ($p < 0.001$). A similar correlation with PD-L1 staining was not observed. Among RCC patients receiving anti-PD-1 therapy, clinical benefit (stable disease or partial response) was characterized by higher CS, regardless of treatment line. When analysis was limited to ccRCC histology, CS were significantly higher ($p < 0.05$) for responders (n = 2) compared to non-responders (n = 4) to nivolumab treatment. **Conclusions:** This is the first study reporting the correlation of a multi-gene score (CS) with immune phenotypes in ccRCC. CS correlates well with intratumor/stromal CD8+ cell infiltration, and is a potential biomarker for response to anti-PD-1 therapy. Consistent with clinical trial data, high CS (associated with poor prognostic tumors) correlated with better responses. Studies with a larger cohort of patients are underway to establish the utility of CS in predicting response to anti-PD-1/PD-L1 therapy.

657 Poster Session (Board #J10), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM

Overall responses with coordinated pembrolizumab and high dose IL-2 (5-in-a-row schedule) for therapy of metastatic clear cell renal cancer: A single center, single arm trial.

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Background: Ligation of IL-2 receptor or blockade of PD-1 receptor may change lymphocytes to induce regression of cancers with diverse histology or site of origin. Single agent objective response rates of 14-25% have been reported for IL-2 therapy of metastatic clear cell RCC (ccRCC). A response rate of 33% was observed in pembrolizumab treated ccRCC patients. Nivolumab treated ccRCC patients were observed to have early intratumoral migration of lymphocytes. A case report of IL-2 induced major regression right after no change on nivolumab therapy suggested that combining the two means of lymphocyte stimulation could be effective. Other trials combining IL-2 receptor agonists (NKTR-214) and PD-1 blockade have also reported regression of ccRCC. Distinctive attributes of high dose IL-2 therapy are the required inpatient stay and the durability of the complete responses. **Methods:** This single-institution, single arm study addresses the safety and feasibility of the combination of IL-2 and pembrolizumab in the treatment of metastatic ccRCC. Subjects are treated on four nine-week blocks, as follows: Pembrolizumab is given on weeks 1, 4, and 7 of each block. Patients are admitted for 5 doses of high dose IL-2 (given over ~ 33 hours/3 days) on weeks 2, 3, 5, and 6 of blocks 2 and 3. Safety is monitored by a Pocock boundary of .05 likelihood of 0.15 dose limiting toxicity rate. The Simon 2-stage alternative hypothesis for the sample size was a 45+% major response rate vs null hypothesis $<$ 20%, at alpha = 0.10, 90% power. **Results:** No accrual stop for safety was triggered. Thirteen of the first 18 patients responded, substantially exceeding the requirement of 8+/24 combination-treated patients to reject the null. Seven patients responded after receiving pembrolizumab alone, six after starting combination therapy in block 2. Accrual is completed; at 27. Kaplan-Meier analysis projects ORR of 69%, with ORR 90%-lower confidence bound of 55%. **Conclusions:** The combination of high dose IL-2 and pembrolizumab is feasible, with a high response rate, justifying further exploration of this dual immune treatment of metastatic ccRCC. Clinical trial information: NCT02964078.

658 Poster Session (Board #J11), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM

Patient perspectives on cytoreductive nephrectomy after CARMENA.

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Background: Conducted over eight years, enrolling 450 patients at multiple centers in Europe, the CARMENA (Cancer du Rein Metastatique Nephrectomie et Antiangiongeniques) trial demonstrated that systemic therapy using sunitinib alone is not worse than cytoreductive nephrectomy (CN) plus sunitinib in metastatic RCC in an intention to treat analysis (hazard ratio HR): 0.89, 95% confidence interval (CI), 0.71-1.10) (Mejean, NEJM, 2018). We wanted to assess patient views related to CN following the publication of these results. **Methods:** The Kidney Cancer Research Alliance (KCCure) conducted a survey among kidney cancer patients. The short survey was created via SurveyMonkey and was disseminated in various patient communities using social media and was posted to the KCCure website in June 2018 after the presentation of the CARMENA trial. Patients were asked "The CARMENA trial presented recently at ASCO found that for kidney cancer patients diagnosed with metastatic disease, there is no overall survival benefit of having a nephrectomy prior to starting systemic therapy. Knowing that information, would you still want to have a nephrectomy at diagnosis if you were metastatic?" Patients were also asked whether they had already had a nephrectomy and their stage at diagnosis, whether they were on systemic therapy, gender and age. **Results:** 186 patients responded with 60.5% being female. Median age 56.5 years (range 26-84). On the question of whether they would want CN. 75.2% of the patients indicated they would still prefer nephrectomy. Of the patients with primary metastatic disease and the tumor in place treated with systemic therapy, 20.1% wanted their kidney tumor to be removed. There was no statistically significant difference between patients who had experience with systemic therapy and those who hadn't, answers were also consistent regardless of gender and age. **Conclusions:** Overall survival should not be overestimated as the most important aim in an end-stage patient population. Patients might think differently about benefits, risks and value of surgical procedures then physicians.

659 Poster Session (Board #J12), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM

Clinical activity of ipilimumab plus nivolumab (Ipi/Nivo) in patients (pts) with metastatic non-clear cell renal cell carcinoma (nccRCC).

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Background: Ipi/Nivo is a standard of care for pts with metastatic clear cell RCC. The clinical activity of Ipi/Nivo in patients with metastatic nccRCC remains poorly defined. **Methods:** Metastatic nccRCC pts who were treated with Ipi/Nivo at Cleveland Clinic or UT Southwestern were retrospectively reviewed. Ipi/Nivo was administered as per CHECKMATE 214. Computed tomography imaging was obtained at baseline and every12 weeks to assess disease response per RECIST 1.1 criteria. Baseline pt characteristics, outcome to therapy and adverse effects as per CTCAE v5.0 were collected. **Results:** Thirteen pts with metastatic nccRCC histology who were treated with Ipi/Nivo were identified. The median age was 60 years (range, 32-81). Non clear cell histologies included adenocarcinoma of renal origin not otherwise specified (2), unclassified (3), papillary (3), chromophobe (3), translocation (1) and medullary histology (1). Nine pts had ECOG PS 0; four pts had ECOG PS 1. Eleven patients were male and two female. IMDC risk group at time of initiation of Ipi/Nivo was favorable (2 pt), intermediate (10 pts) and poor (1 pt). Nine pts received Ipi/ Nivo as first line treatment, three pts received Ipi/Nivo after prior TKI and one pt received Ipi/ Nivo as third line treatment after prior chemotherapy and nivolumab monotherapy. In total, eight pts have thus far undergone restaging scans with three pts demonstrating partial response (PR), one pt demonstrating stable disease (SD) and four pts demonstrating progressive disease (PD). Two pts experienced grade 2 diarrhea, one after 4 cycles and another after 3 cycles of Ipi/Nivo and required prednisone. One pt demonstrated grade 3 hepatotoxicity after 2 cycles of Ipi/Nivo and required prednisone and Mycophenolate Mofetil while another pt demonstrated grade 1 hepatotoxicity after 3 cycles of Ipi/ Nivo requiring prednisone. One pt experienced grade 2 pancreatitis requiring steroids after one dose of Ipi/Nivo. One pt experienced grade 2 fatigue after 1 cycle of Ipi/ Nivo requiring prednisone. **Conclusions:** Ipi/Nivo is feasible and safe in patients with metastatic nccRCC with preliminary evidence of anti-tumor activity. Updated clinical data will be presented.

660 Poster Session (Board #J13), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM

Preliminary results of phase I clinical trial of high doses of seleno-L-methionine (SLM) in sequential combination with axitinib in previously treated and relapsed clear cell renal cell carcinoma (ccRCC) patients.

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Background: The overexpression of hypoxia induced factor 1a/2a in ccRCC leads to up-regulation of vascular endothelial growth factor (VEGF) that results in increased angiogenesis, tumor metastasis, and treatment resistance. Using several preclinical xenograft models, it has been demonstrated that therapeutic doses of the selenium-containing molecules, seleno-L-methionine (SLM) and methylselenocysteine (MSC) caused enhanced degradation of HIF1α/2α, down-regulation of oncogenic miRNA-210 and 155, up-regulation tumor suppressor miRNA-664 and LET-7b, and stabilization of tumor vasculature, yielding higher tumor drug uptake and protection from toxic side effects when combined with chemotherapeutic and VEGF-targeted agents. **Methods:** This is a phase I (3+3 design) dose finding trial of SLM (2500, 3000 or 4000 μg) given orally twice daily for 14 days, followed by once a day in combination with standard dose axitinib to patients with metastatic RCC. Primary endpoint is safety. Secondary endpoint is efficacy including overall response rate (ORR), progression free survival (PFS) and overall survival (OS). **Results:** To date, 12 evaluable patients (pts) with metastatic RCC who progressed on one or more prior lines of treatment were enrolled. The first 3 pts were treated at 4000 μg, the second and third 3 pts were treated at 2500 and 3000 μg respectively. Additional 3 pts were added to 4000 μg. No dose limiting toxicity (DLT) was seen. Most common AEs included fatigue, diarrhea, hypertension, nausea, anorexia, cough, proteinuria and weight loss. Of the 4000 μg cohort, 2 pts achieved CR with ongoing responses at 31 and 29 months, 1 pt had PR for 24 months and 1 had PD at 3 months, 2 pts are not assessed yet. Of the 2500 μg cohort, 1 pt with ongoing PR for 21 months, 1 pt had stable disease for 6 months, and 1 pt had PD at 2 months. The 3000 μg cohort, one pt has ongoing PR for 12 months; another pt had PR lasting 10 months, the 3rd pt had SD for 4 months. **Conclusions:** High dose SLM is safe in combination with axitinib, with promising efficacy. Further data including biomarkers will be presented at the meeting. Clinical trial information: NCT02535533.

661 Poster Session (Board #J14), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM

Associations of rurality and disease outcomes in urologic malignancies.

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Background: Patients residing in rural regions have comparatively worse outcomes for many cancers. However there is less known about treatment and outcome for patients with urologic cancers. The objective of this study is to evaluate differences in treatments and outcomes among patients with urologic malignancies when coming from rural compared to metropolitan communities using national, population-level data. **Methods:** We queried the Surveillance, Epidemiology and End-Results database to identify patients with urological cancers from 1973 to 2015. We compiled patient clinical, demographic, and outcome data, including rurality at the county level. Rural counties is defined as those with $>$ 50% population living in rural areas. We evaluated the association of rurality with treatment received and cancer-specific death using Cox proportional hazard models. **Results:** We identified 989,239 patients including those with Kidney (112,477) Bladder (208,230), Prostate (637,005), and Testis cancer (28,527). Among all, 898,050 (90.4%) were male and 64,992 (6.55%) lived in rural counties. Overall, rural patients were older at cancer diagnosis (mean 70 $\pm$ 12.1 vs 67.41 $\pm$ 12.7) and more frequently of white race (97.1% vs 82.46%) vs urban counterpart. Patients residing in rural counties were less likely to undergo definitive treatment with surgery for stage 1 or stage 2 disease P $<$ 0.001). In multivariable regression, rural status was associated with greater risk of cancer-specific death in kidney cancer (HR: 1.1, 95% CI: 1.02-1.24; P: 0.03) but was not seen in other cancers. Based on % of rurality, adjusted kidney cancer-specific death increased among most rural populations: 15% rurality or more (HR: 1.16, 95% CI: 1.05-1.27; P: 0.03), 40% rurality or more (HR: 1.31, 95% CI: 1.15-1.49; P $<$ 0.001) and 70% or more (HR: 1.32, 95% CI: 1.05-1.67; P: 0.01). **Conclusions:** There are notable differences in cancer incidence, treatment and outcome for patients residing in rural areas. Rural status was associated with poorer cancer-specific survival for kidney cancer but was not seen in other genitourinary malignancies, independent of stage at diagnosis and treatment received. Further research is warranted to understand the factors underlying these differences in outcome.

662 Poster Session (Board #J15), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM

Mechanisms underlying the association between sarcopenia and poor oncologic outcomes in clear cell renal cell carcinoma.

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Background: Sarcopenia (low skeletal muscle mass) is associated with poor outcomes in patients with ccRCC. The mechanisms underlying this association are unclear. To understand this association, we examined gene expression differences by sarcopenic status in patients with ccRCC. **Methods:** The cohort consisted of 62 ccRCC patients treated by nephrectomy and previously transcriptomically-profiled in the Cancer Genome Atlas. Computed tomography scans without contrast performed within two months of surgery were reviewed to determine skeletal muscle cross-sectional area. Sarcopenia (yes/no) was defined according to gender-specific international consensus definitions. Baseline differences in clinicopathologic characteristics were assessed using the Chi-squared test for categorical and t-test for continuous variables. Differential expression analyses were performed using the R package "DESeq2." Gene set enrichment analyses (GSEA) and single-set GSEA were used to evaluate differences in MSigDB Hallmark gene sets and estimate immune cell infiltration, respectively. P-values were corrected for multiple testing (p-adjust). **Results:** The cohort was predominantly male (82%), white (97%) and had localized disease (58%). Median age was 58.9 years (SD: 12.1). Sarcopenic (47%) patients were older ($p < 0.001$), obese ($p < 0.001$), and presented with higher AJCC stage ($p = 0.006$). In primary tumor specimens, sarcopenic patients demonstrated increased expression of angiogenic, inflammatory (e.g., IL-6, TNF-alpha), and epithelial mesenchymal transition programs (p-adjust < 0.05). Furthermore, sarcopenic patients had higher macrophage ($p = 0.003$) and Th17 immune cell infiltration ($p = 0.003$). **Conclusions:** Our findings suggest that ccRCC patients who are sarcopenic harbor gene expression programs associated with more aggressive biology. Increased macrophage infiltration and decreased Th17 immune cell infiltration have been previously associated with worse prognosis in ccRCC. It is not clear whether sarcopenia is a cause or consequence of tumor aggressiveness. Validation of these results in a larger cohort of patients and orthogonal validation are ongoing.

663 Poster Session (Board #J16), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM

Assessment of intratumor heterogeneity using imaging texture features in clear cell renal cell carcinoma.

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Background: Intratumoral heterogeneity (ITH) relates to aggressiveness in clear cell renal cell carcinoma (ccRCC), the most common and aggressive subtype of kidney cancer. Percutaneous biopsies have high diagnostic accuracy. However, ITH lowers their reliability in larger, heterogeneous tumors. Haralick texture features extracted from a gray level co-occurrence matrix (GLCM) is a robust method to assess intrinsic tumor imaging characteristics. Some of these features, including entropy as a measure of ITH, have recently been used in differentiating malignant from benign tumors in various organs. We aim to understand how tumor entropy extracted from magnetic resonance (MR) imaging correlate with tumor grade (aggressiveness) and gene expression heterogeneity in ccRCC. **Methods:** This IRB-approved, prospective study included T2-weighted (T2W) and arterial spin labeled (ASL) MR images of 62 patients with ccRCC. The GLCM was constructed for regions-of interest (ROI) within the tumor and 13 Haralick texture features were estimated. Correlations between texture features and tumor grade were evaluated by logistic regression and quantified by the area under the receiving operating characteristic (ROC) curve (AUC). RNA sequencing of 182 tumor samples in 49 resected tumors was performed. Entropy was correlated with standard deviation (SD) of normalized gene expression levels in multiple samples from the same tumor. Spearman correlation (rho) was computed for each gene. False discovery rate q values < 0.05 were considered statistically significant. **Results:** Entropy was higher in high-grade than low-grade tumors (11.28 ± 0.52 vs. 10.95 ± 0.65) on T2W ($q = 0.028$) and ASL (10.45 ± 1.15 vs. 9.65 ± 1.29) ($q = 0.013$). Entropy had an AUC of 0.70 (T2) for high-grade prediction and was weakly correlated with tumor size ($R^2 = 0.2$). Higher T2 and ASL entropy correlated with higher SD of gene expression. Gene ontology analysis of top correlated genes revealed strong enrichment of genes in metabolic processes. **Conclusions:** Higher MRI entropy predicts high tumor grade and correlates with increased heterogeneity in gene expression of metabolic processes.

664 Poster Session (Board #J17), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM

Genomic and clinical determinants of recurrence in localized clear cell renal cell carcinoma (ccRCC).

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Background: Multiple clinical risk scores and gene expression models have predicted recurrence in localized ccRCC. However, few studies explored genomic alterations (GA) predicting recurrence. **Methods:** We assessed genomic and clinical correlates of disease-free survival (DFS) in surgically treated localized ccRCC using a targeted next generation sequencing (NGS) platform (Oncopanel/PROFILE) and publicly available NGS and clinical data from TCGA. Univariable and stepwise multivariable Cox regression models (stratified by database) were performed. **Results:** 478 patients (123 patients from our institution and 355 patients from TCGA) were included. 150 (31.4%) patients experienced a DFS event (recurrence or death) and 94 (19.7%) died at 3.1 years (yrs) of median follow-up. Median DFS was 6.3 (5.4-7.2) yrs and the 5-yr overall survival rate was 70.8% (64.9-76.7). On multivariable analysis, 4 clinical factors and mutations in 3 genes were significantly associated with recurrence (Table). **Conclusions:** Our study suggests that PTEN, BAP1 and KDM5C GA may improve on clinical factors for prediction of localized ccRCC recurrence. Further work is needed to determine if these GA could improve existing validated risk models.

	Descriptive (N = 478)	Univariable – HR (95%CI)	Multivariable – Adjusted HR (95% CI)
Age, y(95% CI)	60.3 (59.2-61.4)	***1.03(1.02-1.04)***	***1.03(1.01-1.04)***
Sex, N Male(%)	300(62.8%)	1.04(0.74-1.44)	-
T stage, N(%)			
T1a	143(29.9%)	1.00	1.00
T1b	123(25.7%)	1.31(0.77-2.21)	1.07(0.62- 1.84)
T2	53(11.1%)	1.84(0.99-3.39)	1.22(0.61- 2.45)
T3a	115(24.1%)	***3.12(1.94-5.03)***	***1.87(1.07- 3.27)***
T3b-T4	44(9.2%)	***3.87(2.22-6.75)***	***2.19(1.13- 4.23)***
Tumor grade, N(%)			
1-2	231(48.3%)	1.00	1.00
3	195(40.8%)	1.36(0.94-1.95)	0.95(0.65- 1.40)
4	52(10.9%)	***4.61(2.96-7.20)***	***2.57(1.57- 4.20)***
Maximum tumor dimension, cm (95% CI)	6.1(5.8-6.4)	***1.10(1.07-1.14)***	***1.06(1.01-1.10)***
Genomic alterations, N(%)			
P53	10(2.1%)	***2.83(1.04-7.67)***	-
VHL	284(59.4%)	0.97(0.70-1.35)	-
PBRM1	163(34.1%)	0.91(0.64-1.28)	-
SETD2	58(12.1%)	***1.79(1.17-2.73)***	-
KDM5C	34(7.1%)	***1.74(1.02-2.95)***	***2.36(1.38-4.06)***
BAP1	42(8.8%)	***1.70(1.06-2.74)***	***1.69(1.04-2.76)***
PTEN	18(3.8%)	***2.98(1.56-5.71)***	***1.96(1.01-3.81)***
MTOR	24(5%)	1.41(0.76-2.61)	-

665 Poster Session (Board #J18), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM

Tobacco as a possible prognostic factor in advanced renal cell carcinoma.

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Background: It is widely known the causal relationship establised between tobacco use and the development of renal cancer is widely known. Nevertheless, the impact of smoking on the efficacy and safety of anti-angiogenic drugs is unclear. Sunitinib is a tyrosine kinase inhibitor with proven efficacy metastatic renal cell carcinoma (mRCC). **Methods:** A retrospective analysis was carried out including 194 mRCC patients (pts) who received Sunitinib in a single Institution (Hospital Universitario Central de Asturias) with a high incidence of this disease. The aim of this study is to explore the impact of the smoking habit on treatment response in terms of progression-free survival (PFS) and overall survival (OS). **Results:** Most patients presented clear cell histology (92%). Smoking status: 42% (n=82) never-smoker, and 39% (n=76) former-smoker and 19% (n=36) current-smoker. Male predominance 78% (n=145). Median age was 65 (range: 40-84). Survival analysis favors patients with a history of tobacco use. There was no significant difference in PFS between never-smoker vs ever-smoker groups: median PFS 8.13 months (95% IC: 4.75-11.52), vs 12 months (95% IC: 9.97-14.03) was found respectively (p=0,086). Fewer than 10% developed grade 3 toxicity. A significative improvement in OS in patients ever-smokers: median OS 16.23 months (95% IC: 12.22-20.25) vs 26.46 months (95% IC: 16.21-36.73) (p=0.044). The advantage observed in patients with any smoking history became more evident for poor prognosis cases. A median OS 5.03 months (95% IC: 0.84-9.23) vs 14.03 months (95% IC: 7.81-20.26). A median PFS 6.4 months (95% IC: 2.53-10.27) vs 13.33 months (95% IC: 1.14-26.19) $p > 0.05$. **Conclusions:** In this series, tobacco seems to play a role on the efficacy and safety of anti-angiogenic agents in mRCC. However, additional prospective studies in well-balanced populations are required to confirm this data.

666 Poster Session (Board #J19), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM

The impact of PBRM1 mutations on overall survival in greater than 2,100 patients treated with immune checkpoint blockade (ICB).

A. Ari Hakimi, Yasser Ged, Jessica Flynn, Douglas R Hoen, Renzo G Di Natale, Kyle A Blum, Vladimir Makarov, Fengshen Kuo, Maria Isabel Carlo, Chung-Han Lee, Martin Henner Voss, Irina Ostrovnaya, Timothy An-thy Chan, Robert J. Motzer; Memorial Sloan Kettering Cancer Center, New York, NY; MSKCC, New York, NY

Background: PBRM1 is the second most commonly mutated gene in clear cell renal cell carcinoma (ccRCC). We have previously shown favorable outcomes in PBRM1-mutated ccRCC tumors treated with vascular endothelial growth factor (VEGF) inhibitors. Recent data suggested PBRM1 mutations may sensitize ccRCC and non RCC malignancies to ICB therapy. We queried the impact of PBRM1 loss on overall survival (OS) across 2,152 patients treated with ICB. **Methods:** PBRM1 mutations were assessed in metastatic ccRCC patients who received first line (n = 82) or second line (n = 61) ICB or ICB/VEGF combinations. Additionally, 41 cohorts of non-RCC malignancies treated with ICB and combination (n = 2,009) were analyzed. Mutations were assessed by next generation targeted sequencing using archival tissue. Association of mutation status and overall survival (OS) was tested by multivariate Cox regression analysis (MVA) and adjusted for tumor mutation burden (TMB), copy number alterations (CNA), loss of function(LOF) mutations (non RCC cohort) and IMDC risk (for ccRCC patients). **Results:** PBRM1 mutations were not associated with improved OS in ICB the entire ccRCC cohort (HR 1.37; CI 0.79-2.4; p = 0.265), the first line (p = 0.624) or second line setting (p = 0.39) or as combination with VEGF inhibitors (p = 0.2). Several RCC subgroups were investigated (see Table at bottom). In the non-RCC cohorts (n = 2,009) PBRM1 mutations were not significantly associated with OS on univariate analysis (HR = 0.73, p = 0.22 for LOF and HR = 0.84, p = 0.34 for non LOF), and remained insignificant after adjusting for TMB, total CNA, and drug class (CTLA4, PD-1/PDL-1 and combinations) (HR = 1.07, p = 0.78 for LOF and HR = 1.08,p = 0.67 for non LOF). **Conclusions:** Neither in ccRCC nor in the pan-cancer cohort did PBRM1 mutations appear to be associated with improved overall survival with ICB therapy.

	HR (95% CI)	p-value
Risk_Group = Intermediate	1.18 (0.6, 2.32)	0.627
Risk_Group = Poor	4.05 (1.67, 9.85)	0.002
PBRM1 mutated (n = 65)	1.12 (0.62, 2.03)	0.714
1st Line Immunotherapy (n = 82)	0.3 (0.16, 0.55)	< .001

667 Poster Session (Board #J20), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM

Effects of sunitinib and pazopanib on patients physical, social, and emotional function: Result of a prospective patients reported outcome tool.

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Background: Sunitinib and pazopanib are are effective treatment options for metastatic Renal cell carcinoma (mRCC) and both may impair patient's quality of life (QOL). There has been no direct comparison between these agents and their effect on these domains. **Methods:** A prospective study of mRCC patients who had received Sunitinib or Pazopanib as a first line treatment was conducted. A set of questionnaires has been developed in-house, influenced by existing recognised tools, such as EORTC-C 30 and PHQ-9, and is tailored to focus on relevant QoL issues patients face. This questionnaire named as Patient reported outcome tool. They primarily relate to physical, emotional and social functioning in the quality of life of patients. Each category has 4 questions. The questions are quite generic and allow patients to apply them to what's important in their lives. Answers are on a scale of 0-10. The purpose of the questionnaire is to assess a balance of physical, cognitive and independence related aspects of their life over the course of their treatment. All patients are asked to complete the baseline questionnaire and then in every clinical visit. **Results:** Data were collected prospectively of metastatic RCC patients who had received Sunitinib or Pazopanib from May 2017 to Aug 2018. Total 45 patients were included, 23 received Pazopanib and 22 were on Sunitinib. There was a higher rate of significant worsening for the physical well-being subscale for Sunitinib versus Pazopanib. Patients on Sunitinib reported worsening tiredness, skin problems and sleep disturbance. Socially, patients on Sunitinib reported more closer to family, better interaction with friends and more motivated to go out. Problem with feeling sad, fear of death and anxiousness were more pronounced on Pazopanib arm. **Conclusions:** Our study suggested that there are marked differences between Sunitinib vs Pazopanib and their effects on patients physical, emotional and social wellbeing. Physical function was more influenced by sunitnib while pazopanib has more effect emotional wellbeing. Further studies are warranted to confirm these findings.

668 Poster Session (Board #J21), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM

Real-world outcomes of genetic testing in a GU genetics clinic and evaluation of current guidelines.

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Background: Several known hereditary cancer syndromes confer an increased risk for genitourinary (GU)-related malignancies. Various guidelines indicate when to refer patients to genetic counseling for GU cancers, but there are limited data on the performance of these guidelines in clinical practice, and the association between testing outcome and clinical and familial features that may delineate a heritable syndrome. The purpose of this study is to determine the most common indications for ordering genetic testing in a GU Genetics Clinic and evaluate the relationship between the indication for germline testing and outcome. **Methods:** An IRB-approved retrospective chart review was performed for 350 patients seen in a GU Genetics Clinic at a single comprehensive cancer center from 2014-2018. Subgroups of patients were formed based on their indication for genetic testing. Exact binomial tests were used to compare the proportion of patients with a positive (pathogenic or likely pathogenic) germline variant for those with vs. without each indication. **Results:** All patients had a genetic evaluation due to a personal or family history of GU cancer. The majority (324 of 350, 92.5%) were evaluated for either renal cell carcinoma (RCC) or prostate cancer (PrCa). Among patients seen for RCC-related evaluation (n = 159), 23 patients (14.5%) tested positive. Meeting published clinical criteria for a hereditary RCC syndrome significantly predicted positive testing ($P < 0.001$). No other indication for testing, including RCC diagnosis $\leq$ 46 years, predicted for positive germline genetic test results. No positive patients were identified by age of RCC onset alone. Among patients seen for PrCa-related evaluation (n = 173), 13 (7.5%) individuals tested positive; all positive variants were in *ATM* or *BRCA2*. A single patient (1/13) was identified by metastatic PrCa status alone. **Conclusions:** Our data suggest current algorithms lack specificity for selecting individuals with RCC or PrCa at risk for germline mutations, and need to be revised. Evaluation of pedigrees and identifying presence of syndromic features are essential and increase the probability of identifying individuals at risk for harboring a germline mutation.

669 Poster Session (Board #J22), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM

Ipilimumab plus nivolumab (Ipi/Nivo) as salvage therapy in patients with immunotherapy (IO)-refractory metastatic renal cell carcinoma (mRCC).

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Background: Ipi/Nivo is now FDA approved for the first line treatment of patients (pts) with intermediate and poor risk mRCC but activity in IO refractory mRCC patients is still not well reported. Here we seek to report activity of Ipi/Nivo in IO refractory mRCC pts. **Methods:** In this retrospective review, we identified a total of 30 pts with mRCC from 4 academic medical centers across the USA who received salvage Ipi/Nivo after disease progression on IO therapy. Pts with only predominant clear cell histology were captured. Ipi/Nivo was administered as per CHECKMATE 214. Investigator-assessed response rate were noted. Immune related adverse events (irAE) were captured in accordance with CTCAE v5.0. **Results:** The baseline demographics included median age of 60 years (21-82), ECOG PS 0-2, and 73% (22) male and 27% (8) female. IMDC risk categories at the time of salvage Ipi/Nivo initiation were 23% (7), 60% (18) and 3% (1) with favorable, intermediate and poor risk, respectively. The median number of prior systemic therapies was 3 (1-6). Prior IO therapies included nivolumab monotherapy (14), avelumab plus axitinib (3), high dose interleukin-2 (3), pembrolizumab monotherapy (2) and Ipi/Nivo, nivolumab plus hypoxia inducible factor (HIF) inhibitor, atezolizumab plus interferon, atezolizumab monotherapy, pembrolizumab plus bevacizumab, pembrolizumab plus axitinib, varlilumab plus atezolizumab and an oral adenosine inhibitor (1 each). The median time on prior IO therapy was 7 months (1-50), best response was 3% (1) CR, 40% (12) PR, 23% (7) SD and 33% (10) PD. 73% (22) had restaging scans to assess response to ipi/nivo of which 17% (5), 3% (3) and 47% (14) showed PR, SD and, PD respectively. 37% (11) developed any grade irAEs and 6% (2) had grade $\geq$3 irAE including one patient with splenic rupture and one with rash and pneumonitis. **Conclusions:** Ipi/Nivo is feasible and safe in IO-refractory mRCC population with preliminary evidence of anti-tumor activity. Updated response data will be presented.

670 **Poster Session (Board #K1), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM**

Dichotomous sized-based clinical staging of localized renal masses affects management but not clinical outcomes.

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Background: Clinical staging of localized renal masses is assigned according to radiographic tumor diameter cut-offs, with T1 masses defined as 7 cm or less and T2 greater than 7cm. However, it is unknown if tumors with infinitesimal size differences exhibit oncologic behavior to warrant different surgical management. Arbitrarily dichotomizing otherwise similar tumors to different stage groups may inappropriately influence the management of renal tumors and affect patient outcomes. We evaluated differences in management and outcomes in otherwise similarly sized tumors among patients that differ only in clinical T stage. **Methods:** Data from the National Cancer Center Database was extracted on all patients with a diagnosis of stage T1 or T2 clear cell renal cell carcinoma (RCC). Analyses were limited to tumors on the cusp of T1/T2 staging to include: 69 mm, 70 mm, and 71 mm. Clinical data were compared and Kaplan-Meier and Cox proportional hazards survival modeling were performed. **Results:** A total of 2815 patients were included. There were 1882 stage T1 and 933 stage T2 tumors; there were no differences in demographics or comorbidity scores. Of 171 tumors reported to be 69 mm, 132 (77.2%) were staged as T1. Of 2339 70 mm tumors, 1686 (72%) were staged as T1. Of 305 71 mm tumors, 64 (21%) were staged as T1. For management, 11.7% of T1 masses were treated with partial nephrectomy vs 7.3% of T2 masses and 75.8% of T1 masses were treated with radical nephrectomy vs 80.7% of T2 masses ($p<0.001$). T2 masses were more likely to have lymph node dissection than T1 masses (15.1% vs 9.9%, $p<0.001$), but pathologic N and M staging was similar. On survival analyses, there was no difference in survival between T1 and T2 masses. **Conclusions:** In this analysis, tumors of similar size but different clinical stage exhibited similar survival, yet were managed differently according to assigned clinical T stage. Patients with large T1 or small T2 masses may be managed inappropriately if the treatment is based on dichotomized clinical staging alone. When possible, risk calculation using precise parameters such as tumor size as part of a prediction model is preferable to dichotomized rules of thumb when determining optimal treatment courses.

671 **Poster Session (Board #K2), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM**

Analysis of toxicity and clinical outcomes (CO) in full versus reduced dose cabozantinib (cabo) in metastatic renal cell carcinoma (mRCC) patients (pts).

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Background: The full dose of cabo is 60 mg, but some pts are treated with a reduced dose with the clinical anticipation of adverse events (AEs). We compared AEs and CO in mRCC pts treated with full versus reduced dose cabo. **Methods:** We performed a retrospective analysis of 65 mRCC pts treated with cabo at Winship Cancer Institute from 2016-2018. CO were measured by overall survival (OS), progression-free survival (PFS), and objective response (OR). OS and PFS were measured from first dose of cabo to date of death and clinical or radiographic progression, respectively. OR was defined as partial response (PR) or complete response (CR) per RECISTv1.1. AEs were collected from clinic notes. Univariate analysis (UVA) of association between AEs and CO was performed using logistic regression model. **Results:** Most pts were males (68%) and the median age was 63 years. Most (79%) had clear cell RCC (ccRCC) and the majority were IMDC intermediate (59%) or poor (39%) risk. Most pts (68%) received 60 mg and 48% of these pts underwent a dose reduction for AEs. Nearly all pts (95%) who started on a reduced dose experienced AEs, compared to 66% for pts treated with 60 mg. OR rate was similar for pts on 60 mg (18%) and pts on a reduced dose (19%). The median survival was comparable in pts treated with 60 mg and pts treated with a reduced dose (10.9 vs. 8.8 months, p=0.92 for OS and 5.6 vs. 5.1 months, p=0.23 for PFS) per Kaplan Meier estimation. AEs, particularly gastrointestinal (GI) AEs, were associated with significantly lower chance of OR (Table). **Conclusions:** CO may be comparable in mRCC pts treated with full versus reduced dose of cabo, but a reduced dose of cabo may not be associated with decreased AEs. GI side effects may be a poor prognostic factor in mRCC pts treated with cabo. Larger studies are warranted to validate these findings.

UVA of association between AEs and CO.

	OS		PFS		OR*	
Variable	**HR (CI)**	**p-value**	**HR (CI)**	**p-value**	**OR (CI)****	**p-value**
No Toxicity (26%)	1.16 (0.49-2.75)	0.742	0.78 (0.37-1.63)	0.512	4.10 (1.17-14.38)	0.028***
No GI Side Effects (45%)	0.79 (0.36-1.72)	0.549	0.81 (0.44-1.48)	0.484	4.21 (1.16-15.31)	0.029***

*Objective response **odds ratio ***statistical significance at alpha $<$ 0.05

672 Poster Session (Board #K3), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM

Factors linked with receiving a lymph node dissection during surgery for nonmetastatic renal cell carcinoma.

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Background: The benefit of a lymph node dissection (LND) in renal cell carcinoma (RCC) remains poorly defined. Despite this uncertainty, the American Urological Association (AUA) guideline on localized renal cancer recommends that LND be performed for staging purposes when there is suspicion of regional lymphadenopathy on imaging. Using the National Cancer Database (NCDB), we examined factors associated with the receipt of LND at the time of renal surgery. **Methods:** The NCDB was queried for non-metastatic patients who underwent partial nephrectomy or nephrectomy for RCC from 2010 to 2014. Patient socio-demographics, clinical characteristics, and treatment factors were extracted. Logistic regression models were used to examine factors associated with the receipt of LND. **Results:** We identified 110,963 patients who underwent surgery for RCC, of whom 11,867 (11%) had LND performed at the time of surgery. Clinical lymph node (cLN) and pathologic lymph node (pLN) information were available in 11,300 patients, of which 1,725 were preoperatively staged as having positive cLN. In the entire study population, patients who were cLN positive were approximately 19 times more likely to receive a LND at the time of surgery (OR: 18.68, 95%CI: 16.62-21.00). Factors associated with a LND in patients who are cLN negative (n = 106,370) were assessed. Clinical T (cT) stage was the strongest indicator of LND (cT2-4, OR range: 4.87-11.1). Among both cohorts, patients who received surgery at an academic/research institution or traveled farther ($>$ 31 miles) to a treatment center were more likely to undergo a LND. Patients from both cohorts who underwent robotic or laparoscopic surgery were less likely to receive a LND compared to open surgery. **Conclusions:** The greatest predictor of LND receipt is being cLN positive. Among patients who are cLN negative, the greatest predictor of LND is cT stage. Predictors of undergoing LND in all patients and those who are cLN negative include treatment center type and distance to the treatment center. Additional studies to determine the accuracy of clinical staging and assess novel preoperative imaging modalities that evaluate nodal involvement are indicated.

673 Poster Session (Board #K4), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM

Rates of occult brain metastases in patients (pts) with advanced renal cell carcinoma (RCC): A cohort study from patients treated across 22 clinical trials.

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Background: National guidelines for RCC management only recommend brain imaging 'if clinically indicated'; the rate of occult brain metastases is not defined. Early detection of CNS disease has major implications as it typically triggers early intervention with the aim to limit morbidity, including major complications of local progression. In an effort to define the utility of brain screening, we investigated the rate of occult brain metastasis in a large cohort of metastatic RCC pts. **Methods:** We performed a retrospective review of completed and actively accruing metastatic RCC clinical trials conducted at Memorial Sloan Kettering Cancer Center. Individual charts of pts screening for those studies with mandatory brain imaging at baseline were reviewed to identify subjects harboring occult brain metastases. We collected patient demographics, International Metastatic Database Consortium (IMDC) risk status, sites of metastatic disease, and tumor histology. Patients with neurologic symptoms were excluded. Descriptive statistics were applied to analyze findings across the cohort. **Results:** A total of 22 clinical trials for metastatic RCC conducted from 2004-2017 required brain imaging at baseline, and a total of 535 pts were screened in this context. A total of 25/535 pts were found to have occult brain metastasis (4.67%), which was multi-focal in 10/25 (40%) and sub-cm in 15/25 (60%). For these 25 pts, the mean age at diagnosis was 56 years (38-77), and IMDC risk score at enrollment was: 1/24 favorable (4%), 21/24 intermediate (88%), and 2/24 poor-risk (8%) patients. 18/25 patients presented with *de novo* metastatic disease; 13/25 had received prior therapies; and 24/25 patients (96%) had $>$ 2 additional non-CNS sites of metastatic disease at time of screening. 21/23 pts and 2/23 pts were then treated with radiation and surgical resection, respectively. **Conclusions:** This retrospective cohort study shows a 5% rate of occult CNS disease in asymptomatic patients with advanced RCC. These findings can inform current screening guidelines for full disease assessment in metastatic RCC patients.

674 Poster Session (Board #K5), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM

Sarcopenia is independently associated with decreased overall survival after surgery for inferior vena cava tumor thrombus patients.

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Background: The presence of sarcopenia, a lean muscle mass deficiency is independently associated with inferior survival following the surgical treatment of localized renal cell carcinoma (RCC). This association has not yet been studied in more advanced disease such as patients with RCC and concomitant IVC thrombus tumors. In this study we retrospectively examined the association between preoperative sarcopenia and overall survival following definitive surgery for IVC tumor thrombus patients. **Methods:** Baseline lumbar skeletal muscle index (SMI) for patients who underwent surgical treatment for known IVC thrombus tumors between 2006 and 2018 by a single surgeon were quantified at the 3rd lumbar vertebra from preoperative computerized tomography (CT) or magnetic resonance imaging (MRI). The SMI thresholds used to define sarcopenia were developed using ROC analysis of our data and had the most significant relation to overall survival. Overall survival was compared between patients with and without sarcopenia using the Kaplan-Meier method as well as univariate and multivariate cox proportional hazards regression models. **Results:** The cohort consisted of 194 patients of whom 128 (65%) were male and 146 (75%) were non-Hispanic white. There were 143 (74%) clear cell renal cell carcinoma cases. 110 patients (57%) were sarcopenic. Patients with sarcopenia had significantly decreased overall survival, log-rank p=0.009 (Figure). The presence of sarcopenia was also associated with decreased overall survival in univariate analysis, (hazard ratio (HR)=1.80, 95% CI 1.15-2.83; p=0.010). In multivariable analysis controlled for age, number of comorbidities, and AJCC Stage, sarcopenia maintained significance as a predictor of decreased overall survival (HR= 1.66, 95% CI 1.05-2.61; p=0.030). **Conclusions:** Preoperative sarcopenia is independently associated with mortality in patients with IVC thrombus tumors.

675 Poster Session (Board #K6), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM

The genomic landscape of metastatic clear cell renal cell carcinoma (ccRCC) after treatment with systemic therapy.

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Background: The most frequent genomic alterations in patients (pts) with ccRCC have been identified in primary tumors. Here we investigated the genomic landscape of ccRCC in a cohort enriched for metastatic tumors after treatment with systemic therapy. **Methods:** We prospectively enrolled pts with ccRCC in a clinical study in which Whole-Exome Sequencing (WES) of normal and tumor tissue was performed. Clinical features, treatment outcome and survival were evaluated. **Results:** Forty-five pts with ccRCC with a median age of 65 years (range 38–86) were enrolled. According to the Heng risk criteria, 15 pts (33.3%) were classified as favorable-risk 23 pts (51.1%) were intermediate-risk and 7 pts (15.6%) were poor-risk. Pts received a median number of 3 lines (range 0–9) of therapy including cytokines (n=7), anti-VEGF (n=36), mTOR inhibitors (n=10) and/or immune checkpoint inhibitors (n=23). The median progression free survival (PFS) after treatment was 3.5 months (0.7-13.1), 11.1 months (1.1–54.2), 2.7 months (0.7-36.2) and 4.9 months (1.4–29.2) after cytokines, VEGF-, mTOR- and immune checkpoint inhibitors, respectively. The median overall survival (OS) from start of treatment to last follow up was 2.2 years (range 0.2–14.9 years). A total of 68 samples were sequenced. These included 9 (12.5%) primary tumors, 38 (55.9%) collected after treatment with anti-VEGF, 16 (23.5%) after mTOR- and 8 (11.8%) after immune checkpoint inhibitor. VHL, KDM5C, SETD2 and PBRM1 were the most frequent somatic mutations detected in this cohort. In two cases with a short and long response to VEGF targeted therapy (PFS 2.8 versus 50.3 months) rapid autopsies were performed which allowed multiregional (n=7, n=4) sampling. The multiregional sequencing in the rapid autopsy case with a prolonged response to VEGF targeted therapy revealed recurrent KDM5C mutations. **Conclusions:** We present the genomic landscape of metastatic ccRCC after treatment with systemic therapy. We report an increased frequency of KDM5C mutations, previously described to be associated with a favorable response to VEGF-inhibitors.

676 Poster Session (Board #K7), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM

Positive surgical margins after radical nephrectomy for localized kidney cancer: Impact on survival.

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Background: Impact of positive surgical margins (PSM) in patients undergoing radical nephrectomy (RN) in localized renal cell carcinoma (RCC) is poorly understood. We sought to understand the impact of PSM for on overall survival (OS) after RN in clinically localized RCC. **Methods:** Retrospective analysis of patients from the US National Cancer Database who RN for clinically localized (cT1a-cT2b cN0M0) RCC between 2003-13, were stratified into their pathological stage group [pT1a, pT1b, pT2a, pT2b, and pT3a (= Upstaged)] and analyzed by final margin status. Cox Regression Multivariable analysis (MVA) was performed to investigate associations of PSM and covariates on OS. Kaplan-Meier analysis (KMA) of OS was performed for PSM verses NSM for the overall cohort and by stage. **Results:** 37,656 RN events [14312 (38%) pT1a, 13598 (36.1%) pT1b, 6551 (17.4%) pT2a, 2937 (7.8%) pT2b, and 4286 (11.3%) with pT3a upstaging]. PSM rate was 0.9% overall (0.4% pT1a, 0.4% pT1b, 0.4% pT2a, 0.4% pT2b, and 4.7% pT3a upstaged). On MVA for all-cause mortality, PSM was independently predictive for decreased OS (HR 1.51, $p < 0.001$), along with increasing age (HR 1.04, $p < 0.001$), non-Caucasian race (HR 1.199, $p < 0.001$), increasing charlson score (HR 2.23, $p < 0.001$), non-private insurance (HR 1.61, $p = 0.001$), high grade histology (HR 1.21, $p = 0.001$), and sarcomatoid histology (HR 3.61, $p < 0.001$). Pathologic T-stage was also predictive of decreased OS (Referent pT1a, HR 1.17, 1.47, 1.74, and 1.93, for pT1b, pT2a, pT2b, pT3a, respectively; all $p < 0.001$). KMA revealed worsened 5-year OS for PSM vs. NSM for the overall cohort (62.4% vs. 81%, $p < 0.001$), pT2a (61% vs. 79.4%, $p = 0.013$), and pT3a (50% vs. 68.3%, $p < 0.001$) groups. **Conclusions:** PSM is a rare event after RN, but is associated with worsened OS, particularly in pT2 and pT3a upstaged patients. Mechanism of decreased OS cannot be clarified given limitations of the NCDB, these suggest that PSM may pose increased oncologic risks in higher pathological stage. Consideration of further definitive strategies (ex: preemptive wide field resection) may be warranted in select circumstances. Furthermore, our findings call for re-consideration of exclusion of PSM patients from adjuvant therapy trials.

TPS677 **Trials in Progress Poster Session (Board #K8), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM**

Phase II trial of nivolumab (nivo) plus ipilimumab (ipi) in patients with SMARCB1-deficient kidney malignancies.

Pavlos Msaouel, Rebecca Slack-Tidwell, Nizar M. Tannir; University of Texas MD Anderson Cancer Center, Houston, TX; Department of Biostatistics, The University of Texas MD Anderson Cancer Center, Houston, TX; The University of Texas MD Anderson Cancer Center, Houston, TX

Background: The potent tumor suppressor SMARCB1 (also known as INI-1, hSNF5, or BAF47) is inactivated in all cases of renal medullary carcinoma (RMC) and renal cell carcinoma unclassified with medullary phenotype (RCCU-MP), as well as most malignant rhabdoid tumors (MRT) of the kidney. Although rare, these kidney malignancies are highly lethal and often occur in young patients. The role of immune checkpoint inhibitor therapy remains to be prospectively defined in tumors harboring SMARCB1 defects. Although a case report noted efficacy of single-agent Nivo in a patient with RMC (Beckermann et al J Immunother Cancer, 2017), there were no durable responses in subsequent cases (Sodji et al. J Immunother Cancer, 2017). We hypothesize that the combination of anti-PD1 (Nivo) with anti-CTLA4 (Ipi) immune checkpoint inhibitor therapy will lead to more potent antitumor responses compared to those reported with single-agent Nivo. **Methods:** This single-arm phase II trial will test the efficacy of Nivo + Ipi in up to 30 patients with SMARCB1-negative RMC, RCCU-MP, and adult-onset kidney MRTs. Any number of prior therapies is allowed. Patients will be treated with Ipi 1 mg/kg + Nivo 3 mg/kg every 3 weeks x4 doses followed by maintenance Nivo 480 mg every 4 weeks for up to 2 years. Ongoing monitoring for safety and futility will be implemented per the method of Thall et al. (Stat Med, 1995; 14:357-79) using cohorts of 10 patients each. The primary endpoint is objective response rate (ORR) and the trial objective is to achieve a similar or greater ORR compared with the historical ORR of 29% achieved in our institution using conventional cytotoxic chemotherapies. Secondary endpoints include progression-free survival, overall survival, and disease control rate. To evaluate potential biomarkers for treatment response, correlative analyses will be performed in tumor tissue and peripheral blood samples obtained i) pre- treatment (baseline) up to 6 weeks (42 days) prior to initiation of treatment on Day 1, ii) after completion of the combination therapy (Nivo + Ipi) phase, and iii) upon disease progression. At the time of the abstract submission, 2 patients have been enrolled on this study. Clinical trial information: NCT03274258.

TPS678 **Trials in Progress Poster Session (Board #K9), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM**

Phase II trial of ixazomib combined with gemcitabine and doxorubicin in patients with SMARCB1-deficient kidney malignancies.

Pavlos Msaouel, Rebecca Slack-Tidwell, Giannicola Genovese, Najat C. Daw, Arlene O. Siefker-Radtke, Nizar M. Tannir; University of Texas MD Anderson Cancer Center, Houston, TX; Department of Biostatistics, The University of Texas MD Anderson Cancer Center, Houston, TX; The University of Texas MD Anderson Cancer Center, Houston, TX

Background: SMARCB1 (also known as INI-1, hSNF5, or BAF47) is a potent tumor suppressor inactivated in all cases of renal medullary carcinoma (RMC) and renal cell carcinoma unclassified with medullary phenotype (RCCU-MP), as well as the majority of malignant rhabdoid tumors (MRT). These highly aggressive malignancies often occur in young patients (pts) and are associated with poor prognosis. There are currently no approved therapies targeting SMARCB1 defects. We previously showed that SMARCB1 loss induces a synthetically lethal vulnerability to perturbations of the cellular proteostasis machinery by proteasome inhibitors (Genovese et al. Nature, 542:362-366, 2017). The present study was designed to determine whether the addition of the second-generation proteasome inhibitor ixazomib to cytotoxic chemotherapy with gemcitabine and doxorubicin (IGD regimen) can improve outcomes of pts with aggressive SMARCB1-deficient kidney malignancies. **Methods:** This single-arm trial uses the Bayesian optimal phase II (BOP2) design (Heng et al. Stat Med 2017) to determine if the IGD regimen will improve the two co-primary endpoints of objective response rate (ORR) to 50% and 28-week disease control rate (DCR) to 30% compared with the historical ORR and 28-week DCR of 29% and 14%, respectively, achieved using gemcitabine plus doxorubicin alone as first-line or salvage therapy in pts with SMARCB1-negative RMC, RCCU-MP, and adult-onset kidney MRTs treated at our institution. Up to 30 pts aged $\geq$ 12 years old will be enrolled and any number of prior therapies is allowed. Ongoing monitoring for safety and futility will be implemented in 10-patient cohorts. If both the ORR and DCR improve to 50% and 30%, respectively, then there is only a 3.5% chance of stopping early and a 93.1% chance of claiming that IGD is efficacious. Secondary endpoints include progression-free survival, and overall survival. Tissue correlative analyses will be performed to determine whether tumors from pts responding to IGD have increased levels of endoplasmic reticulum stress markers involved in protein turnover. At the time of the abstract submission, 5 pts have been enrolled on this study. Clinical trial information: NCT03587662.

TPS679 **Trials in Progress Poster Session (Board #K10), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM**

Randomized phase II trial of intravenous ascorbic acid (AA) as an adjunct to pazopanib for metastatic and unresectable clear cell renal cell carcinoma (ccRCC): A study of Academic and Community Cancer Research United (ACCRU) GU1703.

Niraj Konchady Shenoy, Fang-Shu Ou, John C. Cheville, Tushar Bhagat, Benjamin Adam Gartrell, Amit Verma, Mark Levine, Lance C. Pagliaro; Mayo Clinic, Rochester, MN; Albert Einstein College of Medicine, Bronx, NY; Montefiore Medical Center/ Albert Einstein College of Medicine, Bronx, NY; National Institutes of Health, Bethesda, MD

Background: AA has re-emerged as a promising anti-cancer agent based on recent knowledge of pharmacokinetics, discovery of unexpected mechanisms of action, and early phase trials with IV AA.(Shenoy et al, Cancer Cell 34: 2018, in press) We hypothesized that ccRCC would be particularly susceptible to anti-cancer effects of IV AA due to: **a.** TET dependent demethylation of the hypermethylated genome of ccRCC causing re-expression of tumor suppressors (Shenoy et al, AACR 2018 Targeting DNA methylation conf. A11; Hu et al, Clin Cancer Res 20:4349-60, 2014) **b.** H2O2 production causing intra-tumoral oxidative damage, hypothesized to be enhanced by high iron content in RCC microenvironment **c.** Intracellular accumulation of dehydroascorbic acid secondary to high HIF activity in ccRCC. Animal data and case reports support the hypothesis. **Methods:** Trial design**:** Patients (pts) with newly diagnosed metastatic/ unresectable ccRCC are randomized 1:1 to arm A (pazopanib 800 mg/d plus IV AA 1g/kg 3 times/week) or arm B (pazopanib 800 mg/d). Protocol treatment is for 10 cycles (unless PD, unacceptable AE, alternative therapy, or pt refusal), each cycle being 28 days. Primary endpoint is Treatment Failure-Free rate at 40 weeks (TFF40). Treatment Failure is defined as: Radiographic disease progression, off-protocol treatment due to AE, alternative therapy initiation (except metastasectomy post clinical benefit), or death. Secondary endpoints include OS, PFS, ORR and AE. Statistical methods: 82 eligible pts (41 in each in arm) will provide 81% power to detect a 19% increase of TFF40 from 45% in arm B to 64% in arm A assuming a one-sided type I error rate of 0.19 (EAST 6.4). Correlatives**:** Epigenetic mechanism: 5mC, 5hmC and H3K27me3 IHC, MeDIP/ hMeDIP seq, RNA seq. H2O2 mechanism: tumor microenvironment iron, tumor catalase IHC. Dehydroascorbic acid mechanism: HIF-1 alpha, HIF-2 alpha, GLUT-1 IHC. Key exclusion criteria**:** G6PD deficiency, renal disease (Cockcroft Gault CrCl $<$ 55 ml/min). ClinicalTrials.gov Identifier: NCT03334409 Status: Open for accrual in 9/10 planned sites. Funding Source: Foundation. Clinical trial information: NCT03334409.

TPS680 **Trials in Progress Poster Session (Board #K11), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM**

An open-label phase II study to evaluate PT2977 for the treatment of von Hippel-Lindau disease-associated renal cell carcinoma.

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Background: In von Hippel-Lindau (VHL), renal cell carcinomas (RCC) are of clear cell histology (ccRCC). HIF-2α has been established as an oncogenic driver in ccRCC, where *VHL* deficiency is the underlying genomic alteration. In this setting, HIF-2α accumulates under normoxic conditions, driving the expression of genes associated with progression of ccRCC, including vascular endothelial growth factor A (*VEGFA*), cyclin D1 and other factors that contribute to tumor growth and proliferation. Management of VHL-associated renal tumors most often involves active surveillance until surgery is recommended for tumors larger than 3 cm to reduce the risk of metastasis. Repeated surgical procedures, which are often required, can carry significant morbidity. Systemic therapy options that can delay or obviate the need for surgery by reducing tumor size are needed. **Methods:** This open-label Phase 2 study will evaluate the efficacy and safety of PT2977, a highly selective small molecule inhibitor of HIF-2α, in VHL patients who have at least 1 measurable ccRCC (per RECIST 1.1). PT2977 will be administered orally at 120 mg once daily. Key inclusion criteria include a germline *VHL* alteration and at least 1 measurable solid ccRCC but no tumor $>$ 3.0 cm requiring immediate surgical intervention. Patients may have VHL-associated tumors in other organ systems. Key exclusion criteria include prior systemic therapy for VHL, evidence of metastatic disease, and history of a non-VHL-associated invasive malignancy in the past 2 years. The primary endpoint is objective response rate (ORR) of ccRCC tumors per RECIST 1.1. Secondary endpoints include duration of response (DOR), time to response (TTR), progression-free survival (PFS), time to surgery (TTS) for ccRCC tumors, and efficacy evaluations for non-ccRCC tumors. Safety and pharmacokinetics of PT2977 will also be evaluated. Patient recruitment is ongoing. Funding: Peloton Therapeutics, Inc. Clinical trial information: NCT03401788.

TPS681 **Trials in Progress Poster Session (Board #K12), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM**

RENAVIV: A randomized phase III, double-blind, placebo-controlled study of pazopanib with or without abexinostat in patients with locally advanced or metastatic renal cell carcinoma.

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Background: Abexinostat is a pan-histone deacetylase (HDAC) inhibitor that has shown promising activity in prior pre-clinical studies and early phase clinical trials. A phase 1b study of pazopanib plus abexinostat (Aggarwal et al. J Clin Oncol 2017) demonstrated strikingly durable responses in patients (pts) with clear cell renal cell carcinoma (RCC), including one patient with previously refractory disease with ongoing response for $>$ 5 years' duration. Induction of histone acetylation in peripheral blood mononuclear cells (PBMCs) was associated with durable treatment response. We hypothesize that the addition of abexinostat to pazopanib will significantly improve outcomes in patients with clear cell RCC. **Methods:** RENAVIV is a global, randomized, double-blind, placebo-controlled, two arm phase 3 study of pazopanib plus abexinostat versus pazopanib plus placebo, in pts with locally advanced or metastatic RCC with clear cell component. Up to one prior line of immunotherapy is allowed. Prior VEGF-targeting tyrosine kinase inhibitor treatment is prohibited. Stratification factors include: 1) Prior immunotherapy (yes/no) and 2) prognostic group (good, intermediate, poor). Pts randomized to pazopanib + placebo have the option of crossing over to receive pazopanib plus abexinostat at the time of disease progression. The primary endpoint is PFS by independent review committee. Secondary endpoints include PFS by investigator assessment, overall survival, safety, objective response rate (ORR), duration of response, patient-reported quality of life, and outcomes in cross-over population. Planned correlative studies include association between histone acetylation and HDAC expression in PBMCs with clinical outcomes. The total planned accrual is 413 pts, estimated to provide 90% power to detect a hazard ratio of 0.67 in the comparison of PFS between experimental versus control arms, with an overall two-sided type I error rate of 0.025. A pre-specified minimum of 50% of patients are required to have received prior immunotherapy. The first patient was enrolled in October 2018. Clinical trial information: NCT03592472.

TPS682 **Trials in Progress Poster Session (Board #K13), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM**

CANTATA: Randomized, international, double-blind study of CB-839 plus cabozantinib versus cabozantinib plus placebo in patients with metastatic renal cell carcinoma.

Nizar M. Tannir, Neeraj Agarwal, Nancy Ann Dawson, Robert J. Motzer, Carmel Maree Jacobs, Toni K. Choueiri, John Stewart Hrom, Daniel M. Geynisman, Nancy B. Davis, Robert A. Figlin, Mary Kathleen O'Keeffe, Jigarkumar R. Parikh, Daniel A. Vaena, Ping-Yu Liu, Bridget O'Keeffe, Xuan Tran, Bernard Escudier; The University of Texas MD Anderson Cancer Center, Houston, TX; Huntsman Cancer Institute, University of Utah, Salt Lake City, UT; Georgetown University Lombardi Comprehensive Cancer Center, Washington, DC; Memorial Sloan Kettering Cancer Center, New York, NY; Auckland City Hospital, Auckland, New Zealand; Dana-Farber Cancer Institute, Boston, MA; Forrest General Cancer Center, Hattiesburg, MS; Fox Chase Cancer Center, Philadelphia, PA; Vanderbilt Ingram Cancer Center, Nashville, TN; Samuel Oschin Comprehensive Cancer Institute, Cedars-Sinai Medical Center, Los Angeles, CA; Winthrop University Hospital, Mineola, NY; Medical College of Georgia, Augusta, GA; The West Clinic, Memphis, TN; Fred Hutchinson Cancer Research Center, Seattle, WA; Calithera Biosciences, Inc., South San Francisco, CA; U1015 INSERM, Gustave Roussy Cancer Campus, Paris Saclay University, Villejuif, France

Background: Glutamine metabolism is upregulated in renal cell carcinoma (RCC) and important for RCC tumor cell proliferation and survival. CB-839 is a first-in-clinic, potent, oral inhibitor of the mitochondrial enzyme glutaminase (GLS), which controls a critical step in tumor cell metabolism of glutamine. CB-839 demonstrated synergistic anti-tumor activity when combined with cabozantinib, a VEGFR2/MET/AXL inhibitor, in preclinical RCC models. In a phase 1 study cohort, CB-839 plus cabozantinib as 2L+ therapy showed encouraging safety and efficacy results, with 50% overall response rate (ORR; RECIST v1.1) and 100% disease control rate in 10 patients with clear cell advanced/metastatic RCC (mRCC). A randomized, double-blind study comparing CB-839 plus cabozantinib vs. cabozantinib plus placebo has been initiated in patients with clear cell mRCC.
Methods: In this ongoing international, randomized, double-blind, multi-center study, enrollment is planned for ~300 patients with clear cell mRCC. To be eligible, patients should have received 1-2 prior lines of systemic therapy for mRCC including ≥1 anti-angiogenic therapy or the combination of nivolumab + ipilimumab, have KPS ≥70%, measurable disease (RECIST v1.1), and no prior cabozantinib (or other MET inhibitor). Patients are randomized 1:1 to receive either CB-839 (800 mg twice daily per oral [PO] route) plus cabozantinib (60 mg daily PO) or cabozantinib plus placebo in 28-day cycles until disease progression or unacceptable toxicity. Patients are stratified by prior PD-1/PD-L1 inhibitor therapy and by IMDC prognostic risk group (favorable vs. intermediate vs. poor). The primary endpoint is progression-free survival (PFS) per RECIST v1.1, determined by blinded independent radiology review. Secondary endpoints are investigator-assessed PFS and overall survival. Safety, response per RECIST, and quality of life are also assessed. Findings of this randomized, international clinical trial will inform the efficacy and safety profile of CB-839, a first-in-clinic metabolic inhibitor, in combination with cabozantinib in patients with mRCC. Clinical trial information: NCT03428217.

TPS683 **Trials in Progress Poster Session (Board #K14), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM**

Phase Ib (COSMIC-021) trial of cabozantinib (C) in urothelial carcinoma (UC) or C in combination with atezolizumab (A) in patients (pts) with UC, castrate resistant prostate cancer (CRPC) or renal cell carcinoma (RCC).

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Background: C is an inhibitor of tyrosine kinases involved in tumor growth, angiogenesis, and immune regulation, including MET, VEGFR, and TAM kinases (Tyro3, AXL, MER). Preclinical and clinical studies suggest that C promotes an immune-permissive tumor environment which may enhance response to immune checkpoint inhibitors (ICI) such as the anti-PD-L1 mAb, A. C is approved for pts with advanced RCC and has shown encouraging clinical activity in combination with a PD-1 targeting mAb in RCC, UC, and CRPC (Nadal et al 2017). A is approved for pts with advanced UC after prior platinum-containing chemo and for chemo-naïve pts with platinum ineligible UC or PD-L1+ cisplatin ineligible UC. Combination of C with A may enhance treatment efficacy in pts with genitourinary (GU) cancers. Here, we present the study design of an ongoing phase 1b trial of C + A which includes cohorts with advanced RCC, UC, and CRPC. **Methods:** This global multicenter, phase 1b, open-label trial will assess the safety, tolerability, activity, and pharmacokinetics of C or C + A (NCT03170960). The study comprises a dose-escalation stage and an expansion stage. The dose-escalation stage (3+3 design) is completed. C 40 mg qd + 1200 mg A q3w is the recommended dose for the expansion stage. In the expansion stage, 18 cohorts (each 30 pts) will be enrolled including 7 cohorts with GU cancers: (1) treatment naïve clear cell RCC; (2) non-clear cell RCC, treatment naïve or following systemic anticancer therapy; (3) UC after prior platinum-based therapy; (4) treatment naïve cisplatin-ineligible UC; (5) treatment naïve cisplatin-eligible UC; (6) UC after prior ICI therapy and (7) CRPC after prior enzalutamide and/or abiraterone. In addition, an exploratory cohort (30 pts) will evaluate single agent 60 mg C in pts with UC after prior ICI therapy. Pts will continue treatment as long as they experience clinical benefit per investigator or until unacceptable toxicity. The primary objective of the expansion stage is the objective response rate per RECIST 1.1 per investigator for each cohort. Secondary objectives will assess safety including immune related AEs. Clinical trial information: NCT03170960.

TPS684 **Trials in Progress Poster Session (Board #K15), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM**

PROSPER: A phase III randomized study comparing perioperative nivolumab (nivo) versus observation in patients with localized renal cell carcinoma (RCC) undergoing nephrectomy (ECOG-ACRIN 8143).

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Background: The anti-PD-1 antibody nivo improves overall survival in metastatic RCC and is well tolerated. There is no standard adjuvant systemic therapy that increases overall survival (OS) over surgery alone for non-metastatic RCC. Priming the immune system prior to surgery with anti-PD-1 has shown an OS benefit compared to a pure adjuvant approach in mouse solid tumor models. The PROSPER RCC trial aims to improve clinical outcomes by priming the immune system prior to nephrectomy with neoadjuvant nivo and continued engagement with adjuvant blockade in patients with high risk M0 RCC compared to surgery alone. **Methods:** This global, unblinded, phase 3 National Clinical Trials Network study is currently accruing patients with clinical stage ≥T2 or node positive M0 RCC of any histology. Tumor biopsy prior to randomization is mandatory to ensure RCC and permits in depth correlative science. The investigational arm will receive two doses of nivo 240mg prior to surgery followed by adjuvant nivo for 9 months (q2 wks x 3 mo followed by 480mg q4 wks x 6 mo). The control arm will undergo standard nephrectomy followed by observation. Randomized patients are stratified by clinical T stage, node positivity, and histology. To enhance accrual and patient quality of life, key upcoming amendments are being instituted. These include biopsy only in the nivo arm, allowance of oligometastatic disease and bilateral renal masses that can be fully resected/ablated, and change of nivo dosing to q4 wks (1 neoadj; 9 adj). With accrual of 766 patients, there is 84.2% power to detect a 14.4% absolute benefit in recurrence-free survival (RFS) at 5 years assuming the ASSURE historical control of ~56% to 70% (HR = 0.70). The study is also powered to evaluate a significant increase in overall survival (HR 0.67). Safety, feasibility, and quality of life endpoints critical to adjuvant therapy considerations are incorporated. PROSPER RCC embeds a wealth of translational work aimed at investigating the impact of the baseline immune milieu, the changes induced by neoadjuvant anti-PD-1 priming, and how both correlate with clinical outcomes. Clinical trial information: NCT03055013.

TPS685 **Trials in Progress Poster Session (Board #K16), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM**

A phase II open-label study of cabozantinib in patients with advanced or unresectable renal cell carcinoma pretreated with one immune-checkpoint inhibitor: The BREAKPOINT trial.

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Background: First-line treatment landscape of metastatic renal cell carcinoma (mRCC) is evolving with strong evidence in favour of PD-1/PD-L1 combinations over tyrosine kinase inhibitors (TKIs). No prospective data about efficacy of TKIs post immune-checkpoint inhibitor (CPI) combinations are available. Among TKIs, cabozantinib has demonstrated progression-free survival (PFS) and overall survival (OS) benefit over everolimus in pre-treated mRCC patients (pts). **Methods:** Overall 49 mRCC pts who received a previous CPI (anti PD-1/PD-L1) will be treated with cabozantinib. Pts will be stratified according to Heng prognostic group, duration of first-line and type of previous therapy received (CPI+CPI or CPI+TKI or CPI+anti-VEGF or CPI monotherapy). Key inclusion criteria include: one previous treatment with a PD-1/PD-L1 inhibitor in first-line and histological diagnosis of clear-cell RCC. The primary endpoint is to assess the efficacy of cabozantinib based on PFS. Secondary endpoints include evaluation of OS, objective response rate and safety profile of the drug. Exploratory endpoints include evaluation of PD-L1 levels by immunohistochemistry in tumor samples; the analysis of the immunological signature/profile of tumor cells; the state of circulating immune cells, as well as the modulating activity of cabozantinib on systemic tumor immunity; the evaluation of bone formation and reabsorption markers in pts with or without bone involvement. Cabozantinib will be administered orally at a dose of 60 mg/day continuously until evidence of disease progression or onset of unacceptable toxicity. Statistical design: By the methodology of Brookmeyer and Crowley, assuming an accrual period of 18 months and a minimum follow-up of 10 months (mos), 49 pts are necessary to detect an increment of the median PFS time from 3.8 mos to 7.4 mos with a power of 90% and one-sided alpha of 5%. The large sample critical value detecting the increment of the PFS median survival time will be 5.54 mos. To date, 2 pts have been enrolled. Clinical trial information: NCT03463681.

TPS686 **Trials in Progress Poster Session (Board #K17), Sat, 7:00 AM-7:55 AM and 12:30 PM-2:00 PM**

Phase II study of sitravatinib in combination with nivolumab in patients undergoing nephrectomy for locally-advanced clear cell renal cell carcinoma (ccRCC).

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Background: Sitravatinib is a receptor tyrosine kinase inhibitor (RTKI) that targets multiple closely related RTK pathways including VEGFR, PDGFR, KIT, MET and the TAM receptors (TYRO3, AXL and MERTK) Nivolumab is a monoclonal antibody against PD-1 and releases PD-1-mediated inhibition of T-cell proliferation and cytokine production. Together, sitravatinib and nivolumab may cooperate to elicit greater anti-tumor activity than either agent alone, as sitravatinib is predicted to enhance several steps in the cancer immunity cycle that may augment nivolumab's efficacy. Mechanisms by which sitravatinib may augment an antitumor immune response include enhanced antigen presentation; depletion of immunosuppressive regulatory T-cells (Tregs) and myeloid-derived suppressor cells (MDSCs) via inhibition of split kinases VEGFR and KIT; and shifting tumor-associated macrophages from an immunosuppressive M2 to a pro-immunogenic M1 phenotype via inhibition of TAM RTKs. Each of these factors converge on promoting T effector cell expansion, tumor infiltration and an antigen-specific anti-tumor immune response. **Methods:** This open-label, non-randomized, preoperative window of opportunity Phase 2 study evaluates tolerability and clinical activity of sitravatinib in combination with nivolumab in pts with locally-advanced ccRCC undergoing nephrectomy. Study treatment consists of 2 weeks of sitravatinib monotherapy followed by 4 weeks of the combination. Sitravatinib is administered orally daily at 120 mg; nivolumab intravenously every 2 weeks at 240 mg. The primary objective is to evaluate clinical activity using percentage of pts achieving a presurgical point-in-time objective response. Secondary objectives include evaluation of safety and tolerability, and determination of the immune effects of sitravatinib monotherapy and the combination through serial tissue and blood collections (temporal changes in PD-L1 expression, selected cytokines and immune cell populations including MDSCs, Tregs and ratio of M1:M2 macrophages). The study is open for enrollment and recruitment is ongoing. Clinical trial information: NCT03680521.